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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

V. LEISHMANIASIS.

General.

Kirk (p. 190) discusses the evolution of the leishmania infections of man pointing out that although three main types of disease are recognized, there is no hard-and-fast line of demarcation between them. He notes that in the Sudan, cases are seen in which the three types merge into, or follow, one another, so that there may be difficulty in differentiating between oriental sore and a primary lesion of kala azar, or between muco-cutaneous leishmaniasis and the mucosal lesions of a post-kala-azar condition. The reason for these variations is that there exist different strains of the parasites which probably have different virulence and tendencies. The leishmania of kala azar in India, the Sudan and the Mediterranean are not identical in all respects—for instance, post-kala-azar dermal leishmaniasis is common in Bengal, but rare in Assam—and there are two well-marked types of oriental sore in Turkestan. Kirk (p. 875) noticed that a monkey which had been inoculated with a strain of leishmania after passage from a human case of kala azar (in the Sudan) through two other monkeys, developed lesions resembling those of espundia. Similar lesions occasionally occur in human kala azar in the Sudan, and may be due to the characteristics of certain strains of leishmania.

Jones *et al.* (p. 543) describe the successful cultivation of leishmania in the yolk sac of developing chick embryos.

Senekjie and Lewis (p. 977) have devised a slide agglutination test with antigens from cultures of the various leishmania, and serum from rabbits immunized first with killed cultures and later with living cultures. Homologous leishmania are agglutinated to high titre, and heterologous to lower titres. It seems that this test may be useful in the diagnosis of human disease.

Visceral Leishmaniasis.

Shortt (p. 100) has written an account of recent research in kala azar, with special reference to Assam.

Epidemiology.

In Tashkent, kala azar shows a remarkable focal distribution within the towns, in spite of the fact that sandflies are uniformly distributed throughout

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

the endemic regions. KHODUKIN (p. 356) attributes this to the existence of reservoir hosts, especially dogs, and he supports this view by aetiological, clinical and epidemiological evidence, noting particularly that whereas in man the parasites are soon eliminated from the peripheral circulation, in dogs they are first present in the extensive multiple papules on the muzzle, and later become generalized in the skin. The dog, therefore, is held to be the principal reservoir of the disease, though there is some evidence of transmission from man to man, and from man to dog. Leishmania have not been found in rats, mice or lizards. BATTELLI *et al.* (p. 977) have found leishmania in the spleen and bone marrow of dogs in Eritrea, and FERRO LUZZI (p. 100) notes that kala azar is endemic in the lowlands of Eritrea.

SEN GUPTA (p. 542) has enquired into the epidemiology of kala azar in Bengal during the period 1931–40, and notes that the distribution of the disease is very unequal. For the whole of Bengal there has been an incidence rate of 210 cases each year per 100,000 of the population ; this is so high that the disease still constitutes one of the grave medical problems.

SCOVEL (p. 875) has written an account of kala azar in China. The point he particularly makes is that the incidence of the disease has increased considerably as a result of disturbances occasioned by war. Kala azar is common in the north, but is almost unknown in the more tranquil south, and the Chinese hold that it follows in the wake of famine, flood and war. CLOW (p. 101) describes kala azar in the Province of Shensi, China, where the disease has now become almost epidemic, and constitutes a serious problem. Sandflies abound in the months of May and June. It is most common in children and young adults, and conforms to the classical type. Treatment consists of administration of various antimonials and of stilbamidine, but of 400 patients, only 31·5 per cent. were cured or doubtfully cured, and 16·3 per cent. relapsed, were moribund or died.

Aetiology : Transmission.

SENEKJIE (p. 359) after a review of available information, concludes that the agent of S. American kala azar, which at first was known as *L. chagasi*, is identical with *L. donovani*.

ARMYTAGE and BOLLIGER (p. 358) have infected a young opossum, while still in the maternal pouch, with *L. donovani*, by intraperitoneal injection.

MALONE and BROOKS (p. 357) argue that the sandfly transmission of kala azar in India has not been satisfactorily established, and quote evidence which, in their opinion, is against this method. For details the original abstract should be consulted. In comment, WENYON expresses the view that the authors have not refuted the sandfly theory, which is receiving increasing support both for kala azar and oriental sore.

Clinical Findings.

LOWE (p. 711) discusses the early diagnosis of kala azar, noting the characteristic feature of irregular fever with rapid pulse but without symptoms of toxaemia. The only other early findings are a positive result with the complement fixation test in which the WKK antigen is used [see SEN GUPTA, below], and the presence of leishmania in sternal puncture material. One condition is essential for early diagnosis, namely, that the possibility of kala azar should be kept in mind.

BURCHENAL and WOODS (p. 635) describe three cases of kala azar in U.S. soldiers who had served in N. Africa and Sicily. In one the only sign was enlargement of lymph glands, particularly of the neck. Biopsy confirmed the diagnosis. Treatment with sodium antimony gluconate was given in all these

cases, with success; stilbamidine was not useful in two of them. ANGEVINE *et al.* (p. 976) report another case in an American soldier, who had served in N. Africa or Sicily, in which the only sign of kala azar was enlarged lymphatic glands, in which the parasites were seen. They describe the histological features of the glands.

If serum from cases of kala azar is kept at 7–11°C. for three days, a precipitate is formed. WERTHEIMER and STEIN (p. 262) show that this is due to a substance, allied to euglobulin, which they have named the Cold Fraction. This phenomenon persists for long periods after clinical cure, and it is not yet known whether, in such cases, cure can be regarded as complete. The fraction is present in certain other morbid conditions.

SEN GUPTA (p. 358) gives an account of the use of the complement-fixation test, with the Witebsky, Klingenstein and Kuhn antigen, for the diagnosis of kala azar. It is usually positive in kala azar, and usually negative in other conditions which might be confused with it, and is very useful for early diagnosis.

Treatment.

Sodium antimony gluconate (Stibatin: Glaxo Laboratories) was used for the treatment of kala azar by BURKE and CHAKRAVARTY (p. 17) with success in each of 21 cases. It is supplied as a solution, of which 1 cc. contains 20 mgm. of pentavalent antimony. The daily dose is 1 cc. for each year of age, with 15 cc. as the maximum, and as much as 100 cc. may be given in 7 days by intravenous or intramuscular injection; there were no unpleasant reactions in this series. FERNÁNDEZ CASTANYS (p. 978) again writes of the successful results obtained in infant kala azar by the use of sodium antimony gluconate suspended in oil and given by the intramuscular route. He thinks that this is the method of choice.

SARROUY and GILLOT (p. 101) report favourably on Pentastib (the methyl-glucamine salt of para-amino-phenyl-stibonic acid) and state that the best results in infant kala azar were obtained when the quantity to be administered was spread over the minimum number of days—*viz.*, for each kgm. of body weight, 0·07 gm. should be injected daily for 4 days, or 0·1 gm. daily for 3 days.

PATEL (p. 263) reports so favourably on Stibatin in kala azar that he regards it as the drug of choice; it has many advantages over neostibosan and urea stibamine. He obtained cure in each of six cases treated.

SEN GUPTA (p. 543) reports cases of mixed kala azar and malaria. Antimonials do not affect malaria parasites, and quinine does not affect leishmania, but there seems to be a certain antagonism between the infections.

It is known that when stilbamidine solution is kept, and especially if it is exposed to light, changes occur which render the substance more toxic. Late sequelae of stilbamidine treatment, observed by KIRK and HENRY (p. 18), were affections of the nervous system (changes in sensation along the course of the trigeminal nerve, neuritis of the nerves of the leg, rarely epilepsy or mania), or fatal delayed poisoning, in coma. These effects did not develop until 1–3 months after the completion of treatment. Stilbamidine is absorbed quickly by the tissues and is released slowly for excretion, and, as HAWKING points out in comment, is in this respect similar to mepacrine. Evidence accumulated that the toxic symptoms were due to chemical changes in the drug, which occur when solutions are exposed to light.

FULTON (p. 19) has investigated the therapeutic action of certain newer aromatic diamidines on *L. donovani* infections of hamsters. For details the original should be consulted. FULLER (p. 264) writes of a colour reaction for aromatic diamidines, previously described by DEVINE, to which he has made certain modifications. Details are given in the original abstract.

Fulton (p. 978) found that penicillin had no action in experimental infection of hamsters with the leishmania of Indian kala azar.

Goodwin (p. 262), in a critical examination, has shown that examination of smears from the cut surface of the spleen of animals infected with *L. donovani*, and counting parasites against cell nuclei, is a reliable method of estimating the progress of the disease and the effect of treatment. It is necessary, however, to count up to 1,000 cell nuclei if the numbers of leishmania are small, in order to obtain a reliable result. The organisms are fairly evenly distributed through an infected spleen.

Cutaneous Leishmaniasis: Oriental Sore.

General. Treatment.

Farooq and Qutubuddin (p. 978) have found oriental sore in as many as 42·68 per 1,000 of the population in part of Hyderabad State; the majority of cases were in children under 10.

Elkerton (p. 543) notes that most of the cases of oriental sore in an Indian Military Hospital were in members of a cavalry unit, or in men engaged in transport and therefore associated with horses. He thinks, therefore, that *Stomoxys calcitrans* may be implicated in transmission. Treatment of these sores by scraping under general anaesthesia, and subsequent dressing with tannic acid powder, was successful, but the injection of atebrin was tried, and was found to have certain advantages.

Kojevnikova (p. 454) has found that the moist type of oriental sore tends to occur on the limbs, and the dry type on the face. The same author (p. 876) describes cases in which oriental sore developed at the site of existing trauma of the skin, and hazards the opinion that sandflies are attracted to such areas in preference to intact skin.

Berberian (p. 877) has shown experimentally that dogs can be infected with *L. tropica*, with the development of cutaneous lesions, but not of visceral lesions. The skin lesions of dogs in nature, which are sometimes attributed only to kala azar, may, in fact, be due to oriental sore.

Bakhrami (p. 454) describes the technique of cultivating *L. tropica* in the chick embryo.

Ball and Ryan (p. 19) quote their experience which shows that Neostam [Burroughs Wellcome & Co.] is very effective in the treatment of oriental sore. Intravenous injections are given twice each week, and increase from 0·05 to 0·2 gm. each, to an average total of about 1·14 gm. Toxic reactions may be reduced by giving the injections at noon, and withholding the midday meal, or they may be controlled by morphine. In 221 American soldiers thus treated, there were no failures; the average time for cure was 14·5 weeks. Neostam seems to be the most effective means of treatment of oriental sore.

Klitzner (p. 455) treated oriental sore with sulphacetamide, and thinks that this drug had some specific action, apart from its effect in eliminating secondary bacterial infection.

Gupta and Kahali (p. 191) have made a pharmacological study of umbellatine, which is derived from *Berberis*, and is allied to berberine. It apparently has a useful action in the infiltration treatment of oriental sore.

Immunization.

Berberian (p. 102) states that the immunity eventually produced by an oriental sore which heals is complete, but he has shown by experiments in man that it takes a long time to develop, about 240 days after inoculation of infective material. During this period, therefore, sores additional to the

deliberately produced sore may be acquired. Immunity does not develop until the papule ulcerates and commences to heal, and the leishmania disappear naturally from the lesion. He (p. 359) has previously found that the incubation period after injection of cultures of *L. tropica* was 2 weeks to 6 months, but he now quotes three cases in which this was as long as 18 to 56 months.

The same author (p. 360) has shown that suspensions of cultivated *L. tropica*, in isotonic saline, will remain viable for 17 days at temperatures varying from 15·8° to 38·3°C. This observation was made to meet the need of physicians who require suspensions for purposes of immunization.

Berberian (p. 360) has attempted to confirm previous work by Pessôa and Pestana, who claimed that inoculation of *L. tropica* killed by phenol would produce immunity to oriental sore. His results were entirely negative, and no immunity to infection was found in two persons so inoculated, though immunity was proved in others who had recovered from sores produced by the injection of living flagellates.

Katzenellenbogen (p. 361) has followed up the results of vaccination in 416 people near the Dead Sea in Palestine, where oriental sore is hyperendemic. The incubation period varies from about 2 weeks to 18 months. In 45 persons a febrile reaction occurred, probably allergic in nature, but in only four of these did a vaccination sore develop. In 27 others no vaccination sore followed, though they had no evidence of previous oriental sore; the possibility of natural immunity is to be considered. The vaccination campaign has produced very favourable results; of 25 persons newly arrived in the district, and vaccinated, none has had a natural sore in a period of 2 years, whereas of 70 not vaccinated, 65 have had sores in the same period.

Muco-Cutaneous Leishmaniasis (American).

Kean (p. 359) states that an endemic focus of cutaneous leishmaniasis has been found in Arraijan, Panama, and describes the clinical features of the disease. A striking feature in several cases seen in the Gorgas Hospital during the present century has been nodular lymphangitis in areas draining the ulcers. Treatment with antimony potassium tartrate or Fouadin is successful. Stewart and Pilcher (p. 712) report a case which they claim to be American muco-cutaneous leishmaniasis, in a boy who had never left Texas.

Costa (p. 544) describes American leishmaniasis in which the lesions may be mistaken for those of yaws.

Lopes and Laender (p. 979) have found that the Montenegro skin test is the method of choice for the diagnosis of mucocutaneous leishmaniasis in the clinics and health centres of the interior of Brazil.

Beltrán (p. 361) has found it impossible, by reducing the *p*H of culture media below 7·2, to eliminate bacteria from cultures of *L. brasiliensis* without killing the leishmania.

Pifano (p. 191) gives a list of sandflies which may be vectors of *L. brasiliensis* in one region of Venezuela.

Pessôa and Villela (p. 712) report favourably on the results of treatment of American muco-cutaneous leishmaniasis with the German preparation "Antimon-ditoxin," which appears to be more useful than tartar emetic and Fouadin. Snow (p. 544) had no success in the treatment of a case of American cutaneous leishmaniasis with penicillin. *Charles Wilcocks.*

MALARIA.

AUSTRALIAN MILITARY FORCES. **Malaria in the Borneo Operations May 1–Sept. 1, 1945** [ENGLISH, J. C., Lt. Colonel, Malariologist Adv. H.Q. AMF.] RFA (46) 4. 16 mimeographed pp. [Med. 5/1.]

——. **Destruction of Adult Mosquitoes in the Early Stages of an Operation** [MACCALLUM, W. P., Brigadier, DDGMS Adv. L.H.Q.] Technical Circular No. 4. 1945, June 6, 4 mimeographed pp. [Med. 45/195/172.]

The incidence of malaria was low in Tarakan. After the landing very few anophelines were found; *A. kochi* was most in evidence. Only two *A. leucosphyrus* breeding places were found, and only one adult *A. umbrosus* was captured. The island is small; its population was static, and mostly congregated near the controlled areas of the oil wells and the port. None of 325 children examined had an enlarged spleen and only two of 225 children harboured malaria parasites, *P. vivax* in each case. Among 600 adults the only positive blood films obtained during a 2-week period were *P. vivax* 21, *P. falciparum* 9 and *P. malariae* 1; all the parasite carriers were Indonesian labourers imported from the mainland by the Japanese.

In Labuan Island before the war mosquito control measures had been limited to an area of 2 square miles in the town of Victoria. The common mosquitoes were *A. kochi*, *A. barbirostris*, *A. hyrcanus*, *A. sundaicus*, *A. leucosphyrus*, *A. tessellatus*, *A. karwari*, *A. separatus*, *A. umbrosus* and *A. philippinensis*. After the arrival of the Japanese mosquito control practically ceased: the tide gates were broken and *A. sundaicus* breeding became common in the town area. Detailed information is lacking regarding the incidence of malaria before the war but *P. falciparum* malaria was said to be rare and cerebral malaria almost unknown. The Japanese imported heavily infected Javanese labour, and used people who had previously lived in a controlled area for clearing and cultivation. Malaria became rife. At the time of the allied landings the spleen rate in Malay children was 75 per cent. During the first 3 weeks of July, some 1,100 of the 8,000 local natives were treated for malaria, amongst whom there were eight cases of cerebral malaria and one of blackwater fever.

In Brunei town malaria had been severe prior to 1935. An antimalaria organization was established in that year and by 1939 the spleen rate in 561 children in the river kampong had been reduced to 1 per cent. On the arrival of the Japanese, the inhabitants of the river kampong fled to the hills and rice-growing districts; some 60 per cent. of them contracted malaria there. They drifted back; malaria control in the town was discontinued, and the incidence of malaria increased. The Japanese also suffered severely, some of them dying from cerebral malaria. *A. kochi* was the commonest mosquito in the town; *A. leucosphyrus* and *A. barbirostris* were common in the outskirts.

In Kuala Belair-Seria there was considerable malaria in 1932. The land was covered with swamp forest, with a narrow sandy coastal strip. The vector was *A. umbrosus*; *A. sundaicus* was not common. As clearing proceeded the latter species replaced the former as the chief vector. Antimalarial work increased in efficiency and there was but little malaria from 1939 to 1941. Other species of mosquito found in this area were *A. kochi*, *A. tessellatus*, *A. separatus*, *A. maculatus*, *A. karwari*, *A. leucosphyrus*, and *A. baezai*. All organized antimalarial work ceased after the Japanese occupation in December 1941. There was an increase of *A. umbrosus* and later of *A. sundaicus* breeding. Native labour was recruited from highly malarious inland villages. In 1944 the malaria rate was higher than it had ever been, even before control work.

Most of British North Borneo was highly malarious ; blackwater fever was not uncommon among Chinese and Malays. Dr. MacArthur found *A. leucosphyrus* to be the chief vector in N.W. Borneo ; it breeds in thick jungle. *A. maculatus* is considered to be unimportant ; *A. umbrosus* and *A. hyrcanus* are said to have been incriminated in certain parts. In Weston, spleen rates of 55 and 54 were found in Malay and Chinese children, respectively.

But little information was available about pre-war malaria in Balikpapan ; the town was well controlled, but the surrounding districts were malarious. After the occupation anophelines taken included *A. sundaicus, A. leucosphyrus, A. leucosphyrus hackeri, A. hyrcanus nigerrimus, A. tessellatus, A. kochi, A. vagus, A. separatus, A. hunteri, A. baezai, A. barbirostris barbirostris, A. novumbrosus, A. albotaeniatus* and *A. montanus* (?). *A. sundaicus, A. leucosphyrus* and *A. hyrcanus nigerrimus* are regarded as vectors in East Borneo ; others are *A. maculatus, A. umbrosus, A. minimus* (on Lacet Island) and *A. hyrcanus sinensis*. A survey of 333 children under 5 years of age, soon after the landing, revealed a spleen rate of 43 per cent. A parasite survey of 277 natives employed as carriers showed *P. vivax* 17 and *P. falciparum* 24.

The incidence of malaria among the troops was low : mepacrine suppression was good. It is not possible to summarize all the control measures employed, but new developments call for note. Of great interest is the information given concerning the destruction of adult mosquitoes by drifting mists. Two types of mist were used, pyrethrum spray from aerosol dispensers, " Freon bombs " and DDT, 2½–5 per cent. in kerosene or distillate. The " Freon bombs " were mostly used indoors, in intact or partly destroyed houses, tunnels, closed pill boxes, etc., but their outside use was also tried. The dosage varied from 4 to 12 seconds' spraying per 1,000 cubic feet. The measure was effective especially against *Aëdes* mosquitoes. The outside use of " Freon bombs " was advantageous in areas of jungle and scrub where *Aëdes* were prevalent. The method adopted was that of walking along bush tracks at the rate of a yard a second with a discharging dispenser in either hand, or of placing them on the ground at 15-yard intervals and allowing them to discharge for 60 seconds at each location.

Five per cent. DDT mist was used only out of doors. The most satisfactory equipment was an American 3-gallon decontaminator pressure sprayer, with a " Rega " nozzle of 0·08 in. aperture. As a means of control against dengue fever, this method appeared to be of the greatest use. The camp area in which a case of dengue occurred, including an area of 100 to 200 yards around it, was thus sprayed.

The use of DDT applied to walls, tents, mosquito nets, etc., for residual effect proved its value.

For larval control in service conditions, the use of plaster of paris and sawdust pellets soaked in 5 per cent. DDT in oil was very convenient and effective. Two parts of sawdust and one part of plaster of paris, by volume, are mixed with water and allowed to set. The mixture is then cut into pellets of from half to one cubic inch and allowed to dry (48 hours). The pellets are then soaked in 5 per cent. DDT in oil for a further 48 hours, and are then ready for use. Their effectiveness was 100 per cent. for 2–4 weeks in suitable breeding places. They may be thrown a considerable distance to breeding places difficult of access, and are ideal for collections of water in bomb craters, tanks, drums, etc., while their use in ricefields is harmless.

The use of suppressive mepacrine prevented malaria incidence being used as an index of the efficiency of mosquito control in the Borneo operations. The very low incidence of dengue, however, among susceptible troops landed in areas where dengue is endemic, is strong evidence of the efficiency of that control. During the first 10 weeks of the operations, there were 44 cases of

dengue in Tarakan, 208 in Brunei Labuan and 85 in Balikpapan. At the end of 10 weeks, very few cases were occurring in any area. The lowest incidence of dengue occurred in the area where most use was made from the earliest days of ground spraying with DDT mists, particularly in camps in which dengue had occurred.

The incidence of malaria was surprisingly low. Up to the end of September only 114 cases of *P. falciparum* malaria had occurred, 55 in Balikpapan, 55 in N.W. Borneo, 4 in Morotai, and 0 in Tarakan, among forces totalling 57,000 during an average period of 12 weeks. *Norman White.*

PAL, R. **On the Bionomics of *Anopheles culicifacies* Giles. Part II. The Ecology of the Immature Stages.** *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 53–74, 1 fig. & 1 chart. [24 refs.]

Part I of this paper was concerned with the longevity of *Anopheles culicifacies* [this *Bulletin*, 1944, v. 41, 448]. In the second part the author discusses the results of his laboratory experiments on the aquatic stages of the mosquito and compares them with observations made in the field.

It is known that *A. culicifacies* breeds in irrigation channels, pools in river beds, borrow pits and cement tanks, and that it can adapt itself to almost any type of water. Experiments showed that there was no consistent preference for any particular type of water. Ovipositing females avoided soapy water, but laid eggs in all the following waters: tap, pond, muddy, tank, irrigation, polluted, stagnant and distilled. The author concludes that eggs are scattered at random, and that this accounts for the presence of *A. culicifacies* larvae in all kinds of breeding places.

Experiments to discover the time of oviposition showed that 60·1 per cent. of eggs were deposited between 19·00 and 22·00 hours, 27·9 per cent. were laid between 22·00 and 01·00 hours and 12 per cent. between 01·00 and 04·00 hours. Thus, egg laying continued throughout the hours of darkness, but most were laid during the first third of the night.

An interesting point of practical value for laboratory workers is that, in captivity, the number of eggs laid at one time by one female *A. culicifacies* varied very little from season to season. The number obtained in these tests is given as 115 to 134.

In the laboratory, ovipositing females showed slight preference for cooler water when given a choice between 38°C. (102·4°F.) and 42°C. (107·6°F.); between 38°C. and 45°C. (113°F.), however, the warmer water was definitely avoided. Eggs, larvae and pupae exposed to constant temperatures between 20°C. (68°F.) and 40°C. (104°F.) indicated that the favourable range for development was between 28°C. (82·4°F.) and 32°C. (89·6°F.) with the optimum at 32°C.

Thermal death points were found to be 53°C. (127·4°F.) for eggs, 45·5°C. (113·9°F.) for fourth stage larvae, and 43·3°C. (109·9°F.) for pupae.

In small natural breeding places the maximum surface temperature during the hot summer months was rarely as high as 44·9°C. (112·8°F.) but 43°C. (109·4°F.) was common. In large ponds it rarely rose above 37°C. (98·6°F.). In May and June, therefore, *A. culicifacies* deserts the hot pools and channels and resorts to the cooler wells and tanks. In December and February the maximum water temperature ranged between 10°C. (50·0°F.) and 15°C. (59·0°F.). At such temperatures the life-cycle takes about three months. In the laboratory, eggs were killed at temperatures below 10°C. and most larvae and pupae died when kept at 5°C. or below.

Results obtained from a long series of experiments to investigate the effects of free and saline ammonia on oviposition and on development of larvae showed

that female *A. culicifacies* laid eggs indiscriminately in concentrations as high as 120 parts per million, but that larvae ceased to develop in concentrations exceeding 12 parts per million. This may partly account for the absence of this anopheline from highly ammoniacal waters.

The effect of organic pollution of breeding places was studied by preparing specially polluted water in the laboratory, withdrawing samples at intervals for analysis, and allowing gravid females the choice of ovipositing in the withdrawn samples. The females and the immature stages were seen to be fairly sensitive to organic pollution. If it exceeded 1064·50 parts per million, females were repelled and larval development ceased.

From several experiments designed to investigate the effect of light and shade on oviposition, the author's conclusion is that shade itself had no appreciable influence, but females were sometimes unable to lay eggs because of the mechanical obstruction caused by the object producing the shade.

Figures relating to the experiments are set out in 13 tables in the text and in five appendices.

Malariologists and entomologists will find this paper a useful contribution to our knowledge of the bionomics of an important mosquito.

H. S. Leeson.

Rao, T. R. **Behaviour of *Anopheles fluviatilis*. Part III. Larvae Habitats in North Kanara District.** *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 77–82.

Nocturnal movements and day-time resting habits of *Anopheles fluviatilis* were dealt with in Parts I and II of this series of papers [this *Bulletin*, 1944, v. 41, 641; 1945, v. 42, 625]. This third paper discusses 9,526 collections of *Anopheles* larvae made in the North Kanara district by the Bombay Provincial Malaria Organization between August 1942 and December 1944.

With the object of obtaining more precise information regarding the breeding places of *A. fluviatilis*, the collection figures were analysed and are presented in two tables.

Altogether 2,557 larvae of *A. fluviatilis* were collected, and of this number 1,678 (65·6 per cent.) were from streams and channels. There were 3,616 searches in streams and channels, and 493 (13·6 per cent.) yielded *A. fluviatilis* larvae. Out of 797 searches in fallow rice fields, 42 (5·3 per cent.), and out of 1,386 in growing rice fields, 102 (7·4 per cent.), yielded *A. fluviatilis* larvae. The species was more prevalent in rice fields in 1944 than in the earlier period. Out of 157 searches in swamps, 40 (25·5 per cent.), produced larvae of this species; though this type of breeding place was relatively uncommon, small and easily dealt with, it should not be ignored. The *kutcha* field wells situated in rice field valleys were also found to be breeding *A. fluviatilis*.

Thus, while it is confirmed that streams and channels are the generally preferred breeding places of this anopheline, the author suggests that intensive studies may reveal that *A. fluviatilis* breeds in rice fields, swamps and wells more commonly than has been believed, and that these places may in some localities be more important even than streams and channels.

H. S. Leeson.

Zolotarev, E. K. [*Anopheles maculipennis* **of Northern Iran.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 50–57, 1 map. [In Russian.]

This paper deals with the distribution and ecology of *Anopheles maculipennis* in Iran. The identification of subspecies was based on the eggs laid by captured females, 5,000 of which produced 1,000 batches of eggs.

It was found that along the Iranian coast of the Caspian Sea, *A. maculipennis* was represented by three subspecies: *typicus*, *subalpinus* and *sacharovi*. *A. m. maculipennis* occurs at the foot of the northern slopes of Elburz and on the eastern slopes of Bagrov Dag and Talish, as well as along a narrow strip of lowlands on the west and east coast. *A. m. subalpinus* is also characteristic for the maritime plains of Sefidrud and Babol, while *A. m. sacharovi* inhabits the steppe zone of the eastern Caspian lowlands and is not found to the west of the town Babolser. As regards the ecological requirements of the different subspecies of *A. maculipennis*, *A. m. maculipennis* is associated with waters originating in the mountains, occurring both at high altitudes and in basins of rivers fed from mountain sources; *A. m. subalpinus* is found in standing waters of the humid maritime lowlands and in rice fields; while *A. m. sacharovi* occurs only in waters of high salinity in the arid steppes. *C. A. Hoare.*

HEILIG, R. **Malaria in Disguise.** *Indian Physician.* 1945, Nov., v. 4, No. 11, 237–43.

This address deals with many pathological conditions that malaria infections may simulate, and some interesting illustrative cases are recorded. The combination of malaria with pneumonia is serious, but sulphonamides and quinine or atebrin can be used simultaneously without giving rise to any untoward effects. A case is recorded which suggests that pleurisy with effusion may be caused by malaria. A patient in whom the symptoms had suggested a diagnosis of coronary thrombosis was found to have a heavy *P. falciparum* infection and was cured with quinine. Malaria may closely simulate amoebic hepatitis, and malaria attacks occasionally present all the features of gallstone colic. The case history of a patient in whom malaria seems to have caused a pylorospasm of allergic origin is of interest. Malarial dysentery, malarial nephritis and malarial ascites are discussed. Cerebral malaria may begin, and end fatally, without any rise of temperature. Persistent hiccough may occur in acute as well as in chronic malaria and only yields to antimalarial treatment. The address ends with the warning that even the heaviest malarial infection does not exclude the possibility of a co-existing appendicitis, puerperal sepsis or urinary tract infection. *Norman White.*

THONNARD-NEUMANN, E. Zur Pathogenese der Malaria-Anämie. [**The Pathogenesis of Malarial Anaemia.**] *Deut. Tropenmed. Ztschr.* 1944, Apr.–May, v. 48, Nos. 7/10, 129–47, 4 figs.

The author studied the blood and bone marrow in 34 cases of malaria, of which 26 were *P. vivax* infections, 7 *P. malariae* and 1 *P. falciparum*. Five cases were natural infections, the rest were induced, all but three by means of blood injections. The patients were allowed 10 paroxysms and then treated with quinine, atebrin or a "new preparation". The clinical picture varied widely; the *P. falciparum* case was fatal.

Daily blood parasite and reticulocyte counts were made. Red blood cell counts and haemoglobin estimations were made twice weekly. In the therapeutic cases, sternal bone marrow was examined four or five times during and subsequent to the malarial attack; the bone marrow was examined once only during the attack in the natural infections.

At the commencement of the infection the mean red blood cell count was 4·5 million per cmm. and the mean haemoglobin value 80 per cent. At the end of the infection the mean red count had fallen to 2·7 million and the mean haemoglobin to 60 per cent. The colour index was estimated in 22 cases of *P. vivax* infection. It was equal to or less than 1 in 15 out of 22 cases on the

first day, greater than 1 in 19 out of 22 at the end of the malarial attack, and equal to or less than one subsequent to treatment. The mean red cell diameter reached a maximum at the height of the infection in the 10 cases of *P. vivax* infection examined (7·65μ compared with 7·3μ on the first day and 7·35μ after treatment).

Before infection the reticulocytes in 20 cases varied between 1 and 14 per thousand red cells. During the malarial attack the reticulocytes did not increase in the peripheral blood, except in one case, in which they reached 25 per thousand red cells. Five days after the commencement of treatment, however, there was a reticulocyte crisis, which in one case reached 175 reticulocytes per thousand red cells. One-third of the cases showed a reticulocyte count of more than 60 per thousand red cells after treatment. Some cases showed a double wave of reticulocytes after treatment, a depression in numbers developing with the temporary reappearance of plasmodia in the peripheral blood.

During the malarial attack the bone marrow showed erythropoietic activity, with a big increase in reticulocytes, which were about eight times as plentiful as in the peripheral blood (the normal ratio of reticulocytes in bone marrow and peripheral blood is given as 3 : 1). Megaloblasts were seen in two cases only, one of which was the fatal malignant tertian infection.

After cure there was a rapid increase of reticulocytes in the peripheral blood, and a corresponding rise in the bone marrow reticulocytes.

In the *P. vivax* cases the infection rate of the reticulocytes in the bone marrow was the same as that in the peripheral blood. The stages of plasmodial development seen in the marrow were the same in proportion as those in the peripheral blood, except that gametocytes were more common in the latter. There was no evidence of increased damage to the reticulocytes in the bone marrow, and the number of plasmodia found in the bone marrow was not greatly in excess of that found in the peripheral blood.

The author considers that the fact that there was no increase in reticulocytes in the peripheral blood during the acute malarial attacks, although during this period the reticulocytes increased in the bone marrow, indicates that the plasmodia must interfere in some way with the discharge of reticulocytes from the marrow into the peripheral circulation. After disappearance of plasmodia from the blood stream this inhibition ceases.

Anaemia in benign tertian and quartan infections therefore developed mainly from the destruction of red cells by the plasmodia, and was associated with an inhibition of the discharge of young red cells from the marrow.

B. G. Maegraith.

Noe, W. L., Jr., Greene, C. C., Jr. & Cheney, G. **The Natural Course of Chronic Southwest Pacific Malaria.** *Amer. J. Med. Sci.* 1946, Feb., v. 211, No. 2, 215–19, 2 charts.

The object of this study was to observe the natural course of relapsing *P. vivax* malaria, acquired in the South-west Pacific, when uninfluenced by specific treatment. It was hoped to ascertain whether or not immunity might develop with sufficient rapidity to justify withholding specific therapy. Seventy-two patients volunteered ; 25 of these received no specific treatment of any sort, at the Hammond General Hospital where the observations were made. Nineteen received specific treatment at some time during the observations, " for administrative reasons only." Seventeen had to receive specific treatment for all clinical activity because of the severity of their infections. Two had parasitaemia only. These patients had previously had from 1 to 16 relapses which had been treated, the average number being 6·64 for 69 patients. They were under observation for 2 to 10 months.

These patients were thus mostly in the chronic relapsing stage of the infection in which frequent recurrences have become well established—Phase 2, as the authors term it. When specific therapy is withheld Phase 2 is characterized by relapses, each of which may include recurrent bouts of chills and fever which tend to assume the single tertian pattern. Each relapse may last from 1 day to more than 3 months. The average duration of 113 untreated attacks was 5·47 days. Between febrile bouts (mouth temperature 100°F. or over) there may be malaise, headache and generalized pains. Parasites are found in the blood during the active periods of this phase. Clinical activity may subside after a single bout of fever, or may recur for months.

During the final stage of the infection (Phase 3) parasitaemia is constantly or irregularly present, but the temperature does not rise above 100°F. An occasional late relapse might occur, though none was noted in this series. Phase 3 lasted for 10 to 80 days in 30 cases which were completely followed; it apparently represents the development of immunity and perhaps cure.

Phase 2 ordinarily lasts many months and Phase 3 many weeks. "Non-specific therapy" is therefore not justified.

The commonly observed cyclic recurrences at regular intervals in chronic South-west Pacific *vivax* infections treated with atabrine [mepacrine] are rarely seen if treatment be withheld. *Norman White.*

ANDREW, R. **A Syndrome in Vivax Malaria probably due to Spontaneous Subcapsular Haemorrhage of the Spleen.** *Med. Jl. Australia.* 1945, Dec. 22, v. 2, No. 25, 460–64.

Among 6,038 patients suffering from *P. vivax* malaria ten developed symptoms strongly suggestive of subcapsular haemorrhage of the spleen. In all, the onset of the syndrome was marked by the sudden occurrence of very acute pain in the left upper quadrant of the abdomen. In four cases pain was also severe in the epigastrium; and in six, pain was referred to the tip of the acromial process of the left shoulder. There was no trauma; six patients were lying in bed when pain seized them; one was awakened by pain, two were sitting down, and one was in the act of swallowing beer. The pain was accentuated by deep breathing and lasted from a few days to many weeks. There was tenderness in the left hypochondrium but no true rigidity. In three cases there were changes at the base of the left lung; friction rub, a small pleural effusion, signs of pulmonary congestion, and complicating pneumococcal pneumonia were all observed. None of the patients was submitted to operation, and all recovered.

All the patients had acquired the malaria infection in New Guinea. The syndrome occurred in three cases before treatment had started; in four cases during treatment; in two cases early in the 6 weeks maintenance course of mepacrine, and in one case three months after an attack of malaria. Five patients had a history of previous malaria; five had none. There was no fever apart from that caused by still active malaria; the pulse rate was not raised except in the first hour or two of very severe pain. The leucocyte counts were normal.

Only one of three conditions appears at all likely to have been the cause of this syndrome—a small rupture of the spleen, a splenic infarct, or a subcapsular haemorrhage of the spleen. In splenic rupture, acute abdominal pain of sudden onset such as characterized these cases, is not common. Moreover, it is unlikely that 10 consecutive cases of rupture of the spleen should have recovered without operative treatment. The blood findings in two patients did not suggest that a haemorrhage of any great size had occurred. The diagnosis of splenic infarct is more difficult to exclude. The shoulder pain, and the symptoms

and signs in the pleural sac and the base of the left lung, are unlikely, however, to have been caused by an infarct. Infarcts in the spleen may occur in malaria without causing signs or symptoms. A sudden stretching of the splenic capsule as the result of haemorrhage is the most likely explanation of the sudden abdominal pain and tenderness. The consequent irritation of the diaphragm would explain the shoulder pain, and the restriction of normal diaphragmatic movement would account for the changes at the base of the left lung. *Norman White.*

Lowe, J. **Malaria contracted after Splenectomy for Splenomegaly probably caused by Kala-Azar.** *Indian Med. Gaz.* 1945, Nov., v. 80, No. 11, 568.

Splenectomy was performed on a male patient who was admitted to a Calcutta hospital in 1944 with an enlarged spleen, the condition being diagnosed as tropical or Bengal splenomegaly; he recovered uneventfully and was discharged in March 1945. A month later he was readmitted with fever which was diagnosed on clinical grounds as due to kala azar, and this diagnosis was supported by the positive result of a complement fixation test made with WKK antigen, and by the response to treatment for kala azar.

In July 1945 he had another attack of fever which lasted for 2 weeks before he came to the School of Tropical Medicine, where his blood showed *Plasmodium vivax*. He was admitted to hospital with a temperature of 104·8°F. and his liver was enlarged down to the level of the umbilicus. Treatment with mepacrine was effective and he was discharged from hospital a week after admission.

The author thinks that the enlargement of his spleen was caused by kala azar which was not diagnosed, that the long duration of malarial fever before treatment was owing to the absence of his spleen and that the great enlargement of his liver during the malarial attack was compensatory for the absence of the spleen. The case indicates that diagnoses of kala azar and malaria should be excluded before splenectomy is done, and that persons whose spleens have been removed should treat malaria with more than ordinary respect.

J. F. Corson.

Howe, C. D. & Duff, F. L. **Effect of Altitude Anoxia in provoking Relapse in Malaria.** *Science.* 1946, Feb. 22, 223.

"In summary, neither relapse nor parasitemia was observed in a group of 50 individuals giving histories of recent malaria within a period of 7 days following exposure to the anoxia produced by a 1-hour stay at 18,000 ft. in a low-pressure chamber."

Lippincott, S. W., Ellerbrook, L. D., Hesselbrock, W. B., Gordon, H. H., Gottlieb, L. & Marble, A. **Liver Function Tests in Chronic Relapsing Vivax Malaria.** *J. Clin. Investigation.* 1945, Sept., v. 24, No. 5, 616–22, 1 fig. [19 refs.]

Liver function tests were carried out in a group of 317 patients during and subsequent to attacks of relapsing *P. vivax* malaria, treated in most cases by atabrine. The tests used were: bromsulphthalein retention after 45 minutes; cephalin flocculation; galactose tolerance, intravenous hippuric acid synthesis; determination of icterus index, and serum bilirubin, serum albumin, globulin, cholesterol and phosphatase, and urinary urobilinogen estimations.

Bromsulphthalein was retained 45 minutes after injection in 4 per cent. of 49 cases in whom the test was made on the second and third day of the malarial attack. Two to forty-four weeks after the attack, 3 per cent. of 149 patients still showed bromsulphthalein retention.

Cephalin flocculation tests were carried out for the first five consecutive days of the acute attack in 42 patients. The results depended to some extent upon the antigens used (Difco and Wilson), but some abnormal flocculation was found.

Galactose tolerance was normal in 4 to 52 weeks after the attack. Hippuric acid synthesis was tested in 56 men following recurrent malarial attacks, and in 26 normal subjects. The malarial subjects showed some slight depression of synthesis. Icterus index and serum bilirubin were increased slightly during the first days of the malarial attack, but were normal after the attack. Urobilinogen was found in the urine at a dilution of more than 1 in 20 during the early days of the attack, but by the fifth day the concentration was within normal limits. The blood proteins were estimated in 172 patients 1 to 26 weeks after an attack; in all, the albumin content was normal, and in three the globulin was raised above 2·7 gm. per 100 cc. Only two patients had lowered total protein.

The authors conclude that there is some evidence of transient disturbance of liver function during recurrent attacks. There is little indication of permanent damage. *B. G. Maegraith.*

Mario, S. **On Three Cases of Idiosyncratic Urticaria in Course of Relapsing Malaria.** *Indian Med. Gaz.* 1945, Nov., v. 80, No. 11, 567.

Perves, M. Observations de paludisme héréditaire et congénital. Paludisme du nourrisson. [**Congenital Malaria.**] *Rev. Paludisme et Méd. Trop.* 1946, Feb. 15, v. 4, No. 23, 33–6.

Rogan, J. M. & Coombes, A. E. R. **Some Aspects of Malaria Therapy on the Eastern Frontier of India 1942–44.** *Indian Med. Gaz.* 1945, Nov., v. 80, No. 11, 572–81.

In 1942 the authors were deputed to investigate the efficacy of the standard army treatment of malaria among troops in the field in Assam. This standard treatment comprised quinine 30 grains daily for 2 days, mepacrine 0·3 gm. daily for 5 days, a "rest" period of 2 days, then pamaquin 0·02 gm. daily (0·03 gm. for British troops) for 5 days.

In an Indian General Hospital in a village in a highly malarious jungle, four methods of treatment were compared: the standard method as above; the standard method using Bayer's atebrin and plasmoquine in place of mepacrine and pamaquin; standard treatment modified by continuing the quinine treatment till fever had subsided; standard treatment modified by commencing with mepacrine and giving 20 grains of quinine daily throughout the 10 days of mepacrine and pamaquin administration. Ninety-two cases were treated by each of these methods, each group containing 43 *vivax*, 32 *falciparum* and 17 mixed infections. The results showed that the standard treatment was effective for the treatment of the acute stage of uncomplicated cases of malaria occurring under war conditions in Assam; there was no evidence that the malaria encountered in Assam was resistant to treatment; there was no appreciable difference between the response of Indian and British troops to treatment; there was no difference between the results obtained with the synthetic drugs of Bayer's and of British origin respectively. The early relapse rates were moderately high; repeated reinfections were probably taking place.

In another series of observations in an Indian General Hospital in Gauhati, Assam, five methods of treatment were compared: (1) the army standard treatment; (2) mepacrine 0·2 gm. every 6 hours for 48 hours, then 0·1 gm. thrice daily for 5 days; (3) mepacrine 0·2 gm. thrice daily for one day, then

0·1 gm. thrice daily for 6 days ; (4) the same treatment as the last, followed by pamaquin 0·01 gm. thrice daily for 3 days ; alkali was given during the mepacrine course to render the urine alkaline before pamaquin was taken ; (5) initial single dose of 0·8 gm. mepacrine followed by 0·1 gm. thrice daily for 7 days. Two hundred patients were treated by each method : they were all Indians. After treatment the patients were sent to a convalescent depot in Shillong, which is malaria-free, for a month's observation.

The results showed that all five methods were about equally effective in controlling fever and parasitaemia ; in the control of fever quinine was slightly more effective than mepacrine in vivax infections, but less so in *falciparum* infections. Irrespective of the treatment used it took ten days and thirty days from the day of admission for the erythrocytes in *vivax* malaria to regenerate to the level found on admission and to five million red cells per cmm., respectively. Corresponding periods for *falciparum* malaria were 25 days and 40 days. [Shillong is 4,500 ft. above sea-level ; blood-counts of healthy residents are likely to be much higher than five million.] No abnormality in total or differential leucocyte counts could be attributed to any of the treatments used. None of the treatments determined the incidence or persistence of albuminuria. Vomiting was the most common sign of intolerance ; this was least common with moderate doses of mepacrine (treatments 3 and 4), and most common in patients treated with an initial dose of 0·8 gm. mepacrine (treatment 5). The standard treatment was the least effective in preventing relapse during the observation period. With the treatments employing mepacrine only, the relapse rate was inversely proportional to the total dosage of mepacrine. Pamaquin after a light mepacrine treatment appeared to reduce the relapse rate.

As a result of these observations the following recommendations were made : that quinine and pamaquin be omitted from the routine treatment, which should consist of mepacrine only, commencing with a moderately high dosage, and that this be followed by suppressive mepacrine treatment.

Norman White.

BURNHAM, R. C. **Acute Atabrine Intoxication: Report of a Case.** *U.S. Nav. Med. Bull.* 1946, Mar., v. 46, No. 3, 434–8.

" A case is described in which acute intoxication by a single dose of more than 90 grains of atabrine resulted in complete recovery without apparent liver damage.

" The patient's suicidal motivation is discussed from the psychiatric viewpoint as representative of a considerable group of suicides."

FITZHUGH, O. G., NELSON, A. A. & CALVERY, H. O., with the technical assistance of J. M. GLASSMAN. **The Chronic Toxicity of Quinacrine (Atabrine).** *J. Pharm. & Exper. Therap.* 1945, Nov., v. 85, No. 3, 207–21, 1 fig. & 1 chart. [17 refs.]

Previous experiments by WRIGHT and LILLIE [this *Bulletin*, 1944, v. 41, 99] and by SIEGEL and MUSHETT [*ibid.*, 1945, v. 42, 178] showed that quinacrine (atebrin, mepacrine) could cause pathological lesions in animals when given in large amounts. It was earlier established that the drug accumulates in the tissues. SCUDI and HAMLIN [this *Bulletin*, 1944, v. 41, 728] reported that rats fed on a high protein, low fat diet were best able to counteract the toxic effects of the drug. When the diet was adequate HEGSTED *et al.* [this *Bulletin*, 1944, v. 41, 649] showed that the addition of certain vitamins gave no increased protection. The present authors have demonstrated differences in the toxic effects produced by giving quinacrine by mouth to albino rats for practically

their whole lifetime, along with a diet high or low in protein. In the main experiment, 180 weanling rats were used in 10 groups of 18. Half of the groups were fed on each diet, while the quinacrine content, calculated as proportion of diet, was 0, 100, 200, 400 and 800 p.p.m. in the different groups. In the case of the higher dosages a start was made at 200 p.p.m. and gradually raised. Each rat was housed individually under controlled conditions of temperature and humidity, and the composition of the diet was defined. The early growth rate was retarded by all dosages of drug, and toxic effects were noted at all levels of administration during the experiment. Periodic studies were made of the blood picture from all groups. The chief change was a leucocytosis, accompanied by an increase in haemoglobin and red cell count, most marked at the highest drug level. Comprehensive microscopic examinations were made of the tissues of over 60 per cent. of the animals. Inanition was a common cause of death in rats receiving a low protein diet and a special study was made of the accompanying changes in the organs of 24 rats. On a diet of 800 p.p.m. one rat lived for 50 weeks ; with 400 p.p.m. on a high protein diet the longest life span was 60 weeks. There was marked damage to heart and liver. The results in a separate experiment with an adequate diet and 400 or 800 p.p.m. of drug were the same as those for the high protein diet. After 18 months' feeding with 200 p.p.m. of drug there was a significant increase in the number of deaths. On the 100 p.p.m. diet some rats lived for 2 years and in both these latter groups microscopic changes in the viscera were slight, the chief organs affected being the heart and liver and to a lesser extent the kidney. The age at which drug treatment was begun did not affect the toxicity of the drug for rats, but there was a significant difference in this respect among different litters. A dose of 100 p.p.m. corresponds to approximately 4 mgm. per kilo. of body weight per day for the rat, and taking time of administration into account, calculation showed that the amount of quinacrine which will produce toxic effects in rats is higher than the therapeutic or suppressive dose for man. A high protein intake reduced the liver damage caused by the highest dose of drug, and cirrhosis of this organ was present in only an insignificant number of cases. At medium dosage levels cardiac damage was noteworthy. After 1½–2 years of drug treatment, anatomical lesions were frequent ; the details given by the authors merit consultation of the original.

J. D. Fulton.

LIPPARD, V. W. & KAUER, G. L., Jr. **Pigmentation of the Palate and Subungual Tissues associated with Suppressive Quinacrine Hydrochloride Therapy.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 469–71.

A slate grey pigmentation of the hard palate, and of the tissue under the nails of hands and toes, has been observed among individuals who have been taking suppressive doses of quinacrine hydrochloride [mepacrine] for some time. Five hundred men, selected at random among medical and surgical patients in a general hospital in the South West Pacific, were examined for this pigmentation. The results were :—

	Months of Suppressive Quinacrine				
	0–6	7–12	13–18	19–24	25–29
Number in group	146	161	124	47	22
Number showing pigmentation ...	0	44	68	30	14
Percent. showing pigmentation ...	0	27·3	54·8	63·8	63·6

The majority of these patients had received a daily dose of 0·1 gm. quinacrine. No pigmentation was observed among patients who had been taking quinacrine for less than seven months. In the hard palate, the pigment varies in colour from slate-grey to blue-black ; it first appears near the mid line, and extends to the gum margins. Under the nails, a slate-grey patch appears near the centre of the nailbed and spreads, but the distal quarter of the nailbed is not affected. In advanced cases the pigmentation may extend into the skin adjoining the nail. There are no associated symptoms, and the average soldier is unaware of the condition. The nails themselves are unaffected. Histological examination of the mucous membrane of the hard palate, and of skin adjacent to a toe nail, showed that the pigment contains iron in an " accessible " form ; it may be haemosiderin. Neither tropical service alone nor previous malaria is a significant factor in the causation of this condition.

Norman White.

Australian Army Medical Research Unit (AIF) Cairns, Queensland [Fairley, N. Hamilton, Director]. **Researches on Paludrine (M4888). A Progress Report [RFA (46) 1].** 1946, Feb., 35 mimeographed pp., 4 charts.

These investigations with Paludrine (N_1-*p*-chlorophenyl-N_5-isopropyl-biguanide acetate) were carried out at Cairns, Australia, on healthy volunteers experimentally infected with New Guinea strains of the three common forms of malaria. For sporozoite-induced infections the transmitting agent was *A. punctulatus* var. *punctulatus*. Soldiers evacuated from New Guinea with overt malaria were also used to test the therapeutic efficiency of the drug. The object of the experiments was to assess the value of Paludrine as (1) a causal prophylactic and suppressive agent, (2) a therapeutic agent, (3) a gametocide, (4) to elucidate its mode of action, especially on e.e. (exoerythrocytic) forms, and (5) to observe any toxic phenomena resulting from its administration.

For the suppressive and causal prophylactic test in *P. falciparum* malaria 17 volunteers received doses of 25 to 100 mgm. of the drug daily, starting from the day previous to the first bites of recently infected mosquitoes, and continuing till 23–28 days after the last infective bites. Some others, who were untreated, or who received mepacrine, acted as controls for mosquito infectivity and for the subinoculations which were made on the 7th day after exposure with 200 cc. whole blood from cases treated with 25 or 100 mgm. Paludrine daily. The volunteers receiving this drug showed no evidence of malaria up to 119 days after therapy ended and the results of the subinoculations were in all cases negative, in contrast to the positive results in the controls. It was concluded, therefore, that Paludrine had acted as a complete causal prophylactic, and thus differed from mepacrine and other drugs. In experiments with *P. vivax* similarly conducted, in which 100 or 300 mgm. of drug were given daily, some comparable results were obtained, but between 37 and 117 days after the last dose all of four volunteers who had received 100 mgm. daily were suffering from malaria. One of six volunteers on the 300 mgm. dosage had parasites in his blood and overt malaria, 19 days after the end of treatment, while five others on the same dosage were free from symptoms up to 118 days after treatment ended. It appeared, therefore, that, in the lower dosage, Paludrine was a partial prophylactic, and that in the higher dosage it was a complete causal prophylactic in 5 out of 6 cases. The 100 mgm. daily dose was adequate for protection against mixed sporozoite-induced infections with *P. vivax* and *P. falciparum* in volunteers, who were subjected to strenuous exercise, chilling, and injections of adrenaline. Malaria due to *P. vivax* developed, however, 24–33 days after the end of drug treatment, as in some previous experiments with this single infection.

For therapeutic purposes the standard course of Paludrine in *P. falciparum* infection was 300 mgm. daily for 10 days. With this treatment, radical cure of 12 out of 12 trophozoite-induced, and of 64 out of 65 sporozoite-induced, infections resulted. Smaller dosages readily brought about rapid disappearance of trophozoites but the clinical response to treatment was not so rapid. The dosage used in *P. vivax* infection varied from a single dose of 100 mgm. to 1·0 gm. daily for 14 days. The clinical response to treatment was not rapid, and showed little variation with the different dosage schedules. Parasites soon became degenerate, but remained in the blood during 5–8 days of therapy, the result being dependent to some extent on the amount of drug given and on the original density of parasites. With the maximum dosage of the drug relapses occurred in sporozoite-induced infections after freedom from malaria for 29–86 days ; but they had not been noted after a considerable period in a few cases treated for overt trophozoite-induced malaria with small doses of drug. The results of treating overt mixed infections were similar to those for the single infections. Of 41 soldiers treated with the standard course of drug for overt *P. falciparum* infection acquired in New Guinea, 12 developed *P. vivax* infections 19–33 days after the last dose of Paludrine, but malignant tertian parasites were absent. In two cases of quartan malaria the clinical response was rapid, but parasites disappeared only slowly. It will be seen therefore that Paludrine proved efficient in the clinical cure of the three forms of malaria, but that the response was not more rapid than with quinine or mepacrine. The radical cure obtained in *falciparum* infections was, according to the authors, " in accord with the concept that there are no persistent e.e. forms in falciparum malaria, and that radical cure will result from therapy with an efficient schizonticide." It appeared that the number of secondary attacks occurring after treatment of sporozoite-induced *P. vivax* infections with Paludrine was smaller than would have been expected had other known antimalarials been used.

Gametocyte production in *P. falciparum* infections appeared to be unchecked by the standard course of Paludrine. The appearance of these sexual forms in the blood remained unchanged during therapy for a period normally observed when treatment with other non-gametocidal drugs is given. The salivary glands of mosquitoes did not, however, become infected, and a considerable amount of experimental evidence was obtained regarding the infectivity of gametocytes for mosquitoes after therapy ended. Blood containing gametocytes was then non-infective for mosquitoes for 4–12 days, depending on the dosage which had been given. The drug appeared to exercise its effect on the growth of the parasite in the insect, and maturation of the oöcysts present was prevented. The gametocytes of *P. vivax* were unaffected in number or morphology by Paludrine. Either development of oöcysts in the mosquito was prevented or chitinization occurred in those partly developed.

Regarding the mode of action of Paludrine, it appeared from a study of the blood parasites in *P. falciparum* infections that the drug affected either the amoeboid forms or a later stage in the schizogonous cycle. This view was confirmed by *in vitro* experiments. It was noted that division of chromatin was arrested, and the asexual cycle thus brought to an end. In studying the action on the (postulated) e.e. forms of this parasite, 30 volunteers were given various doses of Paludrine at different times relative to the bites of infected mosquitoes. Some were fully protected, and from others undergoing treatment blood was subinoculated to fresh hosts on the 7th day after exposure, with negative results, while those in controls were positive. The evidence available to date indicated that Paludrine in certain doses was a true causal prophylactic and that its action was not on the sporozoite but on a later stage in the cycle of development. These results—considered with others, obtained

earlier, in which not all cases of overt malaria from sporozoite-induced infections were cured by certain doses of the drug—lead the authors to believe that the e.e. forms are more susceptible to its action than erythrocytic forms. There is other evidence to support this view. Paludrine also has a powerful action on the maturing schizonts of *P. vivax*. In view of the fact that it was, in general, unable to effect radical cure of this infection produced by mosquitoes, similar inoculation experiments to those above were carried out, and the results indicated that some action took place on sporozoites or e.e. forms, whereby the development of the primary wave of parasites was inhibited. In this respect the drug acts as a causal prophylactic, but not all e.e. forms are destroyed. In certain circumstances it is believed to act as a complete causal prophylactic.

The toxic symptoms which occurred during therapy were few and not of a serious nature. They were associated generally with maximum dosage of 1·0 gm. daily, and included vomiting, diarrhoea and abdominal pain. Red cells, epithelial cells and hyaline casts have been noted in the urine, while in one case there was gross haematuria. These symptoms were readily relieved by withholding or reducing the dose of drug, which has a wide range of effective action, or by clinical cure of the disease. In other cases there was an increase in the myelocytes of the peripheral blood some days after the treatment began, possibly as a result of the drug's action on the bone marrow. *J. D. Fulton.*

Medical J. Australia, 1946, Feb. 16, v. 1, No. 7, 234–6. **Researches on "Paludrine" (M. 4888) in Australia.** From the Land Headquarters Medical Research Unit, Cairns [Fairley, N. H. (Director)].

This is an account of the researches recorded in the paper abstracted above, in addition a short history of the preceding chemotherapeutic investigations is given.

Knowles, F. L. & Fisk, F. W. **DDT Water Emulsion in Rice Fields as a Method of controlling Larvae of *Anopheles quadrimaculatus* and other Mosquitoes.** *Pub. Health Rep.* Wash. 1945, Aug. 31, v. 60, No. 35, 1005–19, 11 figs. (2 on 1 pl.)

Flooded rice fields are often habitats for the larvae of anopheline mosquitoes, but because of their extent and the susceptibility of growing rice to injury, ordinary larvicidal methods are apt to be limited and expensive. The authors have endeavoured to find a safer, effective and cheaper method of controlling the breeding of *Anopheles quadrimaculatus* in rice fields by applying a DDT emulsion to the flooding water, at the pumping station which supplies the water.

The experiments took place in the Stuttgart area of Arkansas, U.S.A., where the flooding water is pumped from deep wells or reservoirs and carried to the fields in canals. The experimental fields were of two sizes, six plots of 12–18 acres each and 30 plots of 1/20th of an acre each. Different kinds of rice were sown in different plots, but the method of culture was the same in all.

To determine the prevalence of mosquito larvae, a sampling routine was established, both in the treated and in the untreated fields. In the six large plots the sampling stations were at varying distances from the water entrance. In the small plots, two sampling stations were located, one at each end. Fifteen negative dips were regarded as sufficient, 20 dips were taken if larvae were scarce and never less than ten if larvae were numerous. After a few days, sampling was done weekly. Larvae of the rice field mosquitoes (*Psorophora confinnis* and *P. discolor*) were common at the beginning of the season and

also after the first flooding, but later, larvae of *Anopheles quadrimaculatus* were most abundant ; larvae of *Culex erraticus* were also present.

The larvicide consisted of DDT (1 part), a solvent (3 parts), and Triton X-100 (1 part). The solvents were : xylol, Culicide B oil, Dendrol or xylol plus Culicide B oil. A description is given (and a diagram) of the apparatus for dispensing the larvicide on the large plots at the rate of 0·1 p.p.m. in the flooding waters at the pump. The delivery rate was checked and recorded every half hour at the outlet. To the small plots DDT was applied individually in concentrations ranging from 100 to 0·1 p.p.m.

Data obtained from 28,000 larval counts are discussed and analysed in nine tables, comparing DDT dosage, solvent, type of plot, distance from water inlet and the counts made in untreated ricefields. The larval counts in the large plots, irrespective of the treatment or the dosages, increased with the distance from the water inlet, thus indicating a loss of toxicity as the water flowed through the canals. Generally speaking, treated fields contained 50 per cent. fewer *Anopheles quadrimaculatus* larvae and 72 per cent. fewer culicine larvae than untreated fields, although the fish *Gambusia* was present in the untreated but not in the treated fields. In the small plots, both anophelines and culicines were completely controlled by DDT concentrations of 1·0 p.p.m. and 0·2 p.p.m., respectively. There was no residual toxicity after one application.

The authors conclude that the addition of DDT to the flooding waters as it enters the ricefields will reduce the breeding of mosquitoes but will not eradicate them. It is considered that the rice suffered no injury from the DDT treatments ; indeed, there was an increase in the rice yield, perhaps as a result of the toxic effect of DDT on the rice water weevil [*Lissorhoptrus simplex*], though this may not be the sole reason. *H. S. Leeson.*

Jones, H. A., Deonier, C. C., Burrell, R. W. & Knipling, E. F. **Larvicidal Aerosols containing DDT.** *J. Econom. Entom.* 1945, Aug., v. 38, No. 4, 432–3.

A mist or aerosol of DDT, prepared by the emission of a DDT in methyl chloride solution from an aerosol cylinder, is lethal to anopheline larvae up to a distance of 60 ft. from the place of emission. Tests were carried out in a very large room in which pans of water were exposed to varying aerosol doses of DDT. Larvae of *Anopheles quadrimaculatus* subsequently placed in pans exposed at 20, 30, 40 and 60 ft. were killed, and it was shown by the subsequent addition of live larvae that the pans at 20 and 30 ft. distance received a sufficient dose of DDT to remain toxic to larvae, despite repeated artificial rain, for a period of 27 days.

Field tests confirmed that the method could be of practical value, and full control was achieved with a dosage of 0·1 lb. per acre on swamps of up to 9,750 sq. ft. *G. Macdonald.*

Wisecup, C. B., Burrell, R. W. & Deonier, C. C. **DDT Sprays Mechanically Dispersed for Control of Anopheline Mosquito Larvae.** *J. Econom. Entom.* 1945, Aug., v. 38, No. 4, 434–6.

A difficulty in the use of DDT as an anopheline larvicide is that the required dose of oil solutions is so small that their regular and even distribution presents technical difficulties. Aerosol bombs have been shown to be a convenient means of distribution, and in the work recorded in this paper the authors tried distribution in the aerosol form with hand atomizers, power sprayers, a large chemical sprayer of the Flit-gun type, knapsack sprayers, and the " decontamination type of spray cylinder." The last two were the most efficient for

the treatment of large, rather inaccessible breeding areas ; they are presumably pneumatic sprayers from which the fluid is ejected by direct air pressure on its surface and is mechanically scattered by a nozzle, stated to be of 56 to 60 gauge orifice, and a whirl plate.

By this means it proved possible to treat very large areas. For instance, in one breeding place 287,100 sq. ft. in extent, full control was achieved up to 500 ft. from the point of application, but the results depended very greatly on the wind—variable, gusty or strong winds interfered with the even deposition of DDT. In consequence, the method is reliable only in the hands of well-trained and observant operators. The authors conclude that distribution in mist form should be of especial value where potholes, hoof-prints, wheel-ruts, and other small depressions provide scattered breeding places, or in breeding areas that are difficult to treat because of depth of water.

[As an anopheline larvicide, DDT will not be used to its full value until means of distribution are devised which take full advantage of the minute doses needed. Both distribution in mists and distribution by discrete application of small doses from an oil-can as described by Ribbands [this *Bulletin*, 1946, v. 43, 409) appear to have definite advantages over more conventional methods, and each will probably have its own sphere of utility. The reviewer hopes that other workers will specify more exactly the type of apparatus used, as colloquial descriptions and trade names are not generally comprehensible.]

G. Macdonald.

Anderson, B. G. **The Toxicity of DDT to Daphnia.** *Science.* 1945, Nov. 23, 539.

This is a note to the effect that DDT in concentrations of 1 to 100 parts per billion [thousand million] of water immobilizes *Daphnia magna*. Less than 1 part per billion is ineffective. These results may be important in relation to the use of DDT for mosquito control, since in many localities it is essential that the zooplankton be protected. *Charles Wilcocks.*

Deonier, C. C. & Jones, H. A. **TDE, 1,1-Dichloro-2,-2-bis (p-Chlorophenyl) Ethane, as an Anopheline Larvicide.** *Science.* 1946, Jan. 4, 13–14.

The compound " TDE " (which differs from DDT in having only two chlorine atoms on the ethane nucleus instead of three) was tested for toxicity to larvae of *Anopheles quadrimaculatus*. The tests were made by comparing TDE and DDT, in (i) acetone suspensions ; (ii) impregnated talc dusts ; and (iii) fuel-oil solutions which were atomized and allowed to settle on the water containing the larvae.

In all tests the TDE appeared to be very slightly more toxic than DDT (except that the " knock-down " with a 0·01 p.p.m. acetone suspension was rather quicker with DDT than with TDE). *J. R. Busvine.*

BLACKWATER FEVER.

Yuile, C. L., Gold, M. A. & Hinds, E. G. **Hemoglobin Precipitation in Renal Tubules. A Study of its Causes and Effects.** *J. Exper. Med.* 1945, Nov. 1, v. 82, No. 5, 361–74, 3 text figs. & 4 figs. on 1 pl. [22 refs.]

The authors review the literature on the question of the genesis of the syndrome of renal failure associated with intravascular haemolysis. They point out that such syndromes all have in common the circulating pigment,

a factor " of vascular or chemical nature " affecting the organism as a whole, and a specific kidney lesion with varying degrees of tubular degeneration and obstruction of tubules by pigmented casts in the convoluted and collecting tubules and ascending loops of Henle.

The theories concerning the cause of the kidney changes in the syndrome are briefly discussed.

The authors investigated the problem by injecting solutions of haemoglobin into rabbits which were secreting acid or alkaline urine and in which the kidney tubules were damaged either by temporary clamping of the renal artery [see SCARFF and KEELE, *Bulletin of War Medicine*, 1944, v. 4, 370] or by the previous poisoning of a specific poison, in this case sodium tartrate.

White domestic rabbits were used and given a diet of rabbit chow and vegetables (for the production of alkaline urine) or oats and stale bread (for the production of acid urine). Water was allowed freely with both diets. The haemoglobin solution was obtained from citrated rabbit's blood. The doses of haemoglobin injected were the equivalents of the amount set free by the lysis of the cells in 200 to 400 cc. human blood. Selective tubular damage was obtained by clamping the renal artery (in previously unilaterally nephrectomized animals) for 15 or 25 minutes, or by the subcutaneous injection of 20 per cent. sodium tartrate in doses of 0·8 to 0·95 gm. per kilo.

Preliminary experiments showed that the injection of the haemoglobin solution into " normal " animals was not followed by evidence of renal dysfunction whether the urine was acid (two animals) or alkaline (two animals).

Following the clamping of the renal pedicle for 15 minutes (the haemoglobin solution was injected 5 minutes before the release of the pedicle) haemoglobin casts were found in the animals with acid urine, but were " not so numerous " in the animals with alkaline urine. In two animals with acid urine there was a pronounced rise of blood urea N after the injection of haemoglobin ; one animal developed temporary oliguria.

When the renal artery was clamped for 25 minutes there was a transitory rise in blood non-protein nitrogen [N.P.N.], which returned to normal in 7 days, with short periods of oliguria and anuria. In the animals with alkaline urine the rise of blood N.P.N. was more persistent, and there was transient oliguria. In two animals with acid urine there was a sharp rise in N.P.N. following haemoglobin injection, and both became anuric. Both died on the fifth day, and there were haemoglobin casts in the tubules in both. A third animal with acid urine showed a rise in N.P.N., without accompanying change in urine volume. This animal was killed on the eighth day and was found to have many haemoglobin casts in the tubules ; the renal pedicle had been clamped a month previously and there was some scarring of the pedicle. The authors suggest that the result obtained may have been due to failure to occlude collateral circulation through the scar tissue.

In the tartrate experiments the degree of renal damage was maximal in the animals secreting acid urine. Haemoglobin casts appeared in both groups of animals after injection of haemoglobin ; they were more numerous in the animals passing acid urine. Blood N.P.N. rose moderately after tartrate injection in both " acid " and " alkaline " animals. There were only minor changes in urinary volume. In the animals injected with haemoglobin subsequent to injection of tartrate, a rise of N.P.N. (above that already produced by the tartrate injection) occurred in one (of 4) " alkaline " animals and two (of 4) " acid " animals. Urinary volume was unchanged in one " alkaline " animal, is not stated in another, and was reduced in two, one animal going into intermittent anuria. The " alkaline " animal showing a rise of N.P.N. died on the fifteenth day ; there were no tubular casts, but there was a high degree of tubular necrosis and some calcification. Urinary volume was reduced in

two of the " acid " animals and in two it is not stated. One animal died in oliguria, the other was killed on the twelfth day; there were many haemoglobin casts in the former and occasional casts in the latter.

The authors conclude from their experimental results that the precipitation of haemoglobin in the renal tubules is not primarily dependent on the reaction of the urine, but on " functional abnormality of individual nephrons," indicated histologically by lesions of the tubules. These alterations in the tubules are non-specific, since they can be produced by either ischaemia or chemical poisoning (tartrate).

Given the combination of renal tubular damage and haemoglobinuria, urinary *p*H may be important, since pigmented (haemoglobin) casts are more common in animals secreting acid urine than in those secreting alkaline urine.

B. G. Maegraith.

BUTTS, D. C. A. **The Rh Factor in Blackwater Fever. A Preliminary Note.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 417–20. [30 refs.]

In this preliminary note the author suggests that a factor concerned in the development of blackwater fever may be isoimmunization to an Rh-like substance present in malarial plasmodia. According to WIENER (quoted as a personal communication) isoimmunization to the Rh factor occurs in 2–4 per cent. of Rh-negative individuals following transfusion with Rh-positive blood or the birth of an Rh-positive foetus. From this the author calculates the possible incidence of blackwater fever per 1,000, using LEVINE'S figures for the incidence of the Rh factor in whites, negroes and Chinese. He compares his calculated results with figures recorded by various authors for the incidence of blackwater fever and erythroblastosis foetalis in whites and negroes. The following table (from the text) summarizes findings :—

	Ratios	
	White	Negroes
(*a*) Cases of blackwater fever (calculated)	30 to 60	9 to 18
(*b*) Cases of blackwater fever. (Deeks and James, 1911)	33 to 59	2·5 to 5·9
(*c*) Deaths from erythroblastosis foetalis	37	2

The figures in the table are misleading. The ratios in line *a* of the table are based on figures giving the incidence of blackwater fever *per* 10,000 *cases of malaria*; those in line *b* are based on figures giving the incidence of blackwater fever *per* 10,000 *of the racial population*. The two sets of figures are therefore not comparable. The author may be excused this error on the grounds of the incredible obscurity of both text and tables in the report by Deeks and James (DEEKS, W. E. and JAMES, D. M., *Report on Haemoglobinuric Fever in the Canal Zone*, I.C.C. Press, 1911, 32), but his figures in line *c* of the table can be due only to bad arithmetic; the real proportion, calculated on the basis of deaths from erythroblastosis foetalis per 10,000 foetal deaths, is nearer 3 to 1 than his figures of 37 to 2 [see POTTER, *Bulletin of Hygiene*, 1941, v. 16, 59]. The rest of the paper deals shortly with aspects of multiple cases of blackwater fever in the same family, stillbirths and blackwater fever, and the rôle of antimalarial drugs in blackwater fever.

B. G. Maegraith.

PETERS, J. T. **Origin and Development of a New Therapy for Crush Injury, Transfusion Kidney and a certain Number of other Diseases.** *Acta Med. Scandinavica.* 1945, v. 123, No. 1, 90–100, 5 figs.

The author states that after an autopsy on a woman who had died of mercuric chloride poisoning he decided to search for " a satisfactory explanation as to how the tubular epithelial cells with almost undamaged glomeruli . . . could produce anuria. Just the reverse would have been expected with such a destruction of the elements of reabsorption." An artificial nephron was constructed and experiments with this suggested that increased intrarenal pressure was an important factor in producing oliguria and anuria.

The author lists 32 diseases, including blackwater fever, in which oliguria or anuria accompanied by uraemic symptoms may occur. He advises decapsulation of the kidneys as an emergency operation in such conditions.

[The paper is diffuse and unconvincing. The author quotes from a letter from the Editor of the *Lancet*, stating that " The treatments which you recommend—decapsulation, diuretics and pressor drugs—are now widely used, separately or in combination."] *B. G. Maegraith.*

TRYPANOSOMIASIS.

RIDLEY, H. **Ocular Lesions in Trypanosomiasis.** *Ann. Trop. Med. & Parasit.* 1945, Oct. 10, v. 39, No. 2, 66–82. [51 refs.]

During the years 1943–44 ophthalmic examinations were performed by the author on 215 West African patients suffering from trypanosomiasis. These patients comprised 39 African soldiers, 44 African civilians (a high proportion of whom were selected on account of past or present eye complaints and whose attendance for ophthalmic examination was arranged), and 132 other African civilians, entirely unselected, who happened at the time to be attending trypanosomiasis dispensaries. Of these 215 patients, 64 were found to have ophthalmic complaints, and 32 of these had lesions of the retina and visual pathway caused by the toxic effects of therapeutic arsenic. Of the remaining 32 who had inflammatory changes in the structure of the eyes, in 10 they were attributable to onchocerciasis, in 14 to miscellaneous injuries and infections, and in only 8 they were regarded as directly due to trypanosomiasis. These eight comprised one patient with nystagmus parkinsonism, with severe mental derangement; two who showed bilateral papilloedema of moderate degree, which was observed to subside during treatment; four in whom the indefinite disk edges and the presence of new connective tissue in the physiological cups and around the central retinal vessels suggested that a similar condition had at one time been present; and only one in whom otherwise unexplained keratitis was found. The keratitis was interstitial and whether or not it was directly due to trypanosomiasis remains in doubt, for it was not possible to examine the eye microscopically for the parasite. The cases with swollen optic disks are confidently reported as papilloedema and not as papillitis, because there was little or no visual impairment even in the acute stage, and because no degree of pallor followed resolution of the swelling. It is possible that the secondary optic atrophy and narrowed retinal vessels reported by observers who had the opportunity of examining the fundus oculi in a large number of untreated patients may in some instances have resulted from chronic papilloedema. Other cases may be due to onchocerciasis.

The supreme importance of onchocerciasis as a cause of ocular inflammations including keratitis, iridocyclitis, choroidoretinitis and optic atrophy in trypanosomiasis patients, is demonstrated by this investigation, and the author has been able, when visiting trypanosomiasis clinics in the Gold Coast, to find unsuspected cases of ocular onchocerciasis and to confirm the diagnosis by the demonstration of intraocular microfilariae. Onchocerciasis is without doubt the predominant cause of ocular inflammations in trypanosomiasis subjects.

The miscellaneous lesions require little comment, being such as might occur in any series of inhabitants of the African bush.

The following conclusions are drawn from the author's observations :—

1. In man, inflammations due to the presence of trypanosomes within the tissues of the eye are rare, and as yet no case has been proved by microscopical examination. The substantia propria of the cornea is the part most likely to be affected.

2. Such inflammations are practically confined to the terminal stages of the disease, shortly preceding death. Intraocular trypanosome infection cannot be regarded as a common or important cause of impaired sight in Africa.

3. Ocular abnormalities are found in uncomplicated trypanosomiasis, but these are secondary to infection of the meninges and central nervous system and resemble those found in other forms of lymphocytic meningo-encephalitis. The commonest of these is papilloedema, which may develop in the acute stage of infections of only moderate severity. More rarely, ophthalmoplegias, Argyll-Robertson pupils and nystagmus occur.

4. Concurrent onchocerciasis is common and ophthalmologically important. This disease in all probability accounts for the majority of cases of intraocular infections, keratitis, iridocyclitis, choroidoretinitis and very possibly optic atrophy when occurring in untreated cases, previously attributed to trypanosomiasis.

5. The risk of amblyopia, and even amaurosis, from therapeutic arsenic is serious. *E. O'G. Kirwan.*

Nelson, J. W. **The Treatment of Rhodesian Trypanosomiasis with Penicillin.** *East African Med. J.* 1945, Dec., v. 22, No. 12, 407–8.

The patient was a man in an advanced stage of Rhodesian sleeping sickness unlikely to live for more than a few weeks if no treatment were given, while treatment with the usual drugs would have been useless ; penicillin was therefore tried.

He was in a stuporose state, unable to answer questions and incontinent ; the superficial lymph glands were not enlarged ; very slight oedema of the legs was present. Trypanosomes were numerous in the blood and cerebrospinal fluid and the latter showed 0·1 per cent. of protein and 566 cells per cmm., 96 per cent. being lymphocytes. Other blood findings were : erythrocytes 5,360,000 ; haemoglobin 12·6 gm. (90 per cent. Sahli) ; formol gel +10 minutes, opacity ++ ; serum proteins 8·8 gm.—albumin 3·4 gm., globulin 5·4 gm. ; Kahn reaction negative ; E.S.R. 97 mm. in 1 hour, 117 mm. in 2 hours.

He was treated with penicillin as follows : 20,000 units i.m. every 3 hours for 7 days ; 40,000 units i.v. on the first day ; 20,000 units intrathecally on the 2nd and 6th days ; total, 1,250,000 units in 8 days.

Trypanosomes were found in the cerebrospinal fluid on the 2nd day [of treatment ?], but not on the 6th day nor after death, which occurred on the 16th day after admission ; they were present in the blood throughout. After death the cerebrospinal fluid contained 0·5 to 1 unit of penicillin per cc.

The author concludes that the administration of penicillin had no effect on *Trypanosoma rhodesiense* in this case. [See also this *Bulletin*, 1945, v. 42, 453 ; 1946, v. 43, 112.] *J. F. Corson.*

VAN HOOF, L., LEWILLON, R., HENRARD, C., PEEL, E. & RODJESTVENSKY, B. **A Field Experiment on the Prophylactic Value of Pentamidine in Sleeping Sickness.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 327–9.

This field experiment was referred to in a previous paper [this *Bulletin*, 1944, v. 41, 928] ; it was begun in December 1942 in two villages—Iwangu and Mukwamene—of the Kwango District of the Belgian Congo. The district was heavily infected with Gambian sleeping sickness and the density of *Glossina palpalis* was high but the infectivity rate of the flies was not determined. There were 1,124 inhabitants of the villages and in 1942, before the experiment was begun, 99 new cases and 70 old cases of sleeping sickness were known there. These 169 persons together with some [21] temporarily resident persons were excluded from the experiment, leaving 934 ; of these, 721 were given an injection of pentamidine, 3 mgm. per kgm. body weight, and the other 213 were left as controls, receiving no injection. The controls were so distributed among the families as to make the risk of infection as even as possible.

The treated persons and the controls were periodically examined during the next 14 months, thick blood films being taken from all, enlarged lymphatic glands being punctured, and lumbar puncture being done in some of them. In July 1943 a second injection—4 mgm. per kgm. of isethionic acid pentamidine salt—was given to 370 of the 679 treated persons who were examined on that date.

The following table, compiled from the authors' data, shows the results :—

TABLE

Date	Treated persons		New cases	Controls	
	Number	Pentamidine mgm. per kgm.		Number	New cases
Dec., 1942 ...	721	3		213	
Mar., 1943 ...	694		0	200	6 (3%)
July, 1943 ...	679 ⎫ 370 ⎭	4	0	194	1 (0·5%)
	⎧ 309		0		
Nov., 1943 ...	332 (1 inj.)		4 (1·2%)	184	1 (0·5%)
	361 (2 inj.)		0		
Feb., 1944 ...	331 (1 inj.)		4 (1·2%)	193	1 (0·5%)
	354 (2 inj.)		1 (0·3%)		
Total ...	721		9 (1·2%)	200	9 (4·5%)

All the 18 infected persons diagnosed during the examinations were found, by lumbar puncture, to have normal cerebrospinal fluid. [This suggests that the infections were acquired during the period of the experiment, though it does not exclude the existence of inapparent (" cryptic ") infections in others whose cerebrospinal fluid was not examined.]

The authors conclude that the results are better than those obtained with Bayer 205 [see this *Bulletin*, 1935, v. 32, 8 ; 1936, v. 33, 657 ; 1940, v. 37, 703] and that in the field a single dose of 3 mgm. per kgm. body weight of pentamidine (4 mgm. of the isethionic salt) injected intramuscularly would protect

a healthy person from sleeping sickness for at least 6 months. [Only three among the 194 controls showed infection between March 1943 and February 1944; a carefully planned and controlled experiment with volunteers and isolated infected flies might reduce the unknown factors—exposure to infection, virulence of strains, individual resistance, influence of repeated bites, etc.—or at least disclose them.] *J. F. Corson.*

Morris, K. R. S. **A Large-Scale Experiment in the Eradication of Tsetse (*Glossina palpalis* and *G. tachinoides*).** *Farm & Forest.* Ibadan. 1944, v. 5, No. 4, 149–56, 1 map. [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, Feb., v. 34, Pt. 2, 18–19.]

Sleeping sickness in the Gold Coast is most serious in the savannah forest country of the Northern Territories and is associated with *Glossina palpalis*, R. D., and *G. tachinoides*, Westw., which also play a major part in the transmission of animal trypanosomiasis there. Their widespread distribution throughout the populated areas hampers the development of animal husbandry. *G. morsitans*, Westw., occurs over more than half of the Northern Territories, but is confined to sparsely populated country, of which it checks the development. *G. palpalis* and *G. tachinoides* are strictly riverine in the savannah country, and the climate is extremely unfavourable to them for several months of the year. It was therefore thought that it might be possible to control them sufficiently to eradicate trypanosomiasis by the clearing of fly-belt vegetation. This was begun in 1928 on the eastern cattle route and continued at Pong Tamale. Clearings for the control of sleeping sickness were begun in 1930, but work was interrupted from 1931 until 1937 and only conventional clearing was done in the intervening years. This consisted of the formation of protective clearings, designed to exclude tsetse from such places as waterholes and road and river crossings, where transmission of animal trypanosomiasis and sleeping sickness was thought to be taking place. They were found to be unsatisfactory because transmission is seldom confined to a definite, restricted area, they have never completely excluded the flies, which have been shown to travel as much as five miles along rivers in the wet season, they cause undesirable concentration of people and stock and the abandonment of land otherwise good, their upkeep requires constant effort, and the removal of all woody vegetation from an area may cause erosion of river banks, with consequent silting up of the cleared water holes so that the people are driven to uncleared river for their water.

Because of these considerations, it was decided, when anti-tsetse work was resumed in 1937, to concentrate research on the eradication of the fly. *G. palpalis* and *G. tachinoides* extend more or less continuously along water courses during the rains, but retire to well-defined, localised foci during the dry season. These foci consist of definite plant associations, and the removal of the trees and shrubs concerned in every dry-season focus throughout a whole river system results in the disappearance of these two species of *Glossina*. The work is quick and inexpensive compared with previous practices and has an immediate effect. If it is done from the headwaters downwards and very thoroughly, the essential species of fly-belt vegetation are removed throughout the river system and re-introduction upstream is unlikely. The effect is therefore permanent.

A large-scale experiment in tsetse eradication along these lines has just been completed in Lawra district, in the north-western corner of the Northern Territory. This district, two-thirds of which is drained by the Kamba River, a major tributary of the Black Volta, forms part of a wild area of endemic sleeping sickness containing local epidemic centres and continuous with th

most serious sleeping sickness region in French West Africa. The whole of it had become involved in a gradually spreading epidemic by 1930, and consequent depopulation was still in progress in 1938, through both mortality and movement of the frightened people away from the rivers. This migration had serious secondary results, as it caused over-stocking of the poorer land and allowed *G. morsitans* to spread into the depopulated areas. Clearings at some of the most highly infected villages were made in 1939, and the large-scale eradication programme was started on the Kamba River system in 1940. It was supplemented by a sleeping-sickness survey and mass treatment of the whole of Lawra district in the first half of 1941. By the end of the second dry season (March 1942), all the primary fly foci on the Kamba and its tributaries had been eliminated. This involved 105 miles of clearing in a total of 250 miles of river and tributaries. In 1943 and 1944, 60 miles of clearing were added on the neighbouring streams. At the same time, effort was concentrated on the eradication of the fly-belt vegetation on the Kamba, and at the end of 1944 more than half of the river was permanently reclaimed. On the completion of the Kamba clearing in 1942, the heavy communities of *G. palpalis* and *G. tachinoides* were eliminated. Routine catches at five observation points along the river during the wet season produced totals of less than five flies for the whole period of 1943, as against over 4,000 in the neighbouring uncleared Volta, and 2,100–5,000 per year at the same points before clearing. Clearing of the Kamba and neighbouring tributaries of the Volta has now freed 1,000 sq. miles of country from *G. palpalis* and *G. tachinoides*. A small amount of migration upstream from the uncleared Volta occurs, but this has not been found to extend beyond the lowest five miles of cleared rivers. The admission rate of new cases of sleeping sickness at Lawra hospital in the first half of 1944 showed a reduction of 90 per cent. on that in 1938. Development of the reclaimed land is progressing satisfactorily, and incidental advantages are reduction in the populations of lion, leopard and hyaena because of the removal of their favourite cover in riverine fringing forest and the opening up of good stretches of river for fishing.

G. morsitans appeared in the Kamba valley in 1940. The observation in East Africa that it lives in sparsely-inhabited, uncultivated bush and depends on large antelope for food, has been confirmed in the Gold Coast. Although it sometimes feeds on man and cattle, it never occurs in well-populated districts. Resettlement of the depopulated Kamba areas should, therefore, drive it out. However, because of its alarmingly rapid rate of increase, measures were immediately taken to control it by breaking up the large herds of game and reducing their numbers. Operations were begun on the upper river and gradually extended downstream. It had completely disappeared on the upper reaches of the river by 1944, and its numbers along the central Kamba were greatly reduced.

Data are given on the cost of the measures described against all three species, and the direct and indirect advantages of eradicative clearing are shown. Appendices contain lists of the trees and shrubs invariably associated with the presence and breeding of *G. palpalis* and *G. tachinoides* in the dry season and of those forming secondary, wet-season habitat in the north, but probably forming dry-season habitat in coastal savannah or transition forest, and notes on the procedure with regard to each group and on clearing technique.

LITTLE, P. A. & SUBBAROW, Y. **A Practical Liquid Medium for Cultivation of *Trypanosoma cruzi* in Large Volumes.** *J. Bacteriology.* 1945, July, v. 50, No. 1, 57–60, 1 fig.

The authors describe a liquid medium for the cultivation of *Trypanosoma cruzi* in large volumes. It consists of a solution of peptone, glucose and sodium

chloride in contact with coagulated rabbit erythrocytes. Amounts of 50 to 100 mgm. red cell solids per 5 ml. of solution, 5 gm. per 50 ml., and 50 gm. per 5 litres produced the best results, the number of trypanosomes in culture varying from ½ to 1 million per ml.

The red cell coagulum is prepared as follows: 100 ml. volumes of fresh rabbit blood are poured into 1 litre volumes of boiling distilled water, mixed thoroughly and kept boiling for 10 minutes until coagulated. The hot coagulum is collected on cheesecloth filters, while the yellow filtrate is discarded. When semi-dry, the coagulum is transferred to trays lined with absorbent paper, the drying process being continued for 48 hours in a 37°C. incubator. The coagulum is stirred occasionally to aid the formation of small granules. When dry the granules can be sifted and ground finer with mortar and pestle and stored indefinitely. They are soluble in normal sodium hydroxide.

The exact method of preparation of the medium varies according to the purpose for which it is required, and is fully described. In all cases a measured amount of dry granulated red cell coagulum is placed at the bottom of a glass vessel, and a solution containing 20 gm. peptone+5 gm. sodium chloride+2 gm. glucose per 1 litre distilled water is added. This medium can be used for maintenance of cultures, for the assay of chemotherapeutic agents and for the preparation of trypanosome antigens. Cultures of *T. cruzi* in this medium are first incubated at 28°C. for about a week and later kept at room temperature. Maximum growth is obtained in 5–8 days, the culture remaining satisfactory for a fortnight.

Promising results were obtained with some other proteins, especially with thrombin when used with ferric protoporphyrin. *C. A. Hoare.*

LEISHMANIASIS.

Tchernomoretz, I. **The Tissue Culture of L.D. Bodies of *L. donovani* and *L. infantum* from Flagellates.** *Harefuah.* Jerusalem. 1946, Feb. 15, v. 30, No. 4. [In Hebrew 87. English summary 89.]

"Colonies of L.D. bodies of Leishmania in vitro were first obtained on medium (agar-locke-serum) made up with specific immune serum (Adler & Theodor, 1926). Mixed cultures of L.D. bodies and flagellates were obtained by Weinman (1939) on medium (agar-tyrode-serum) to which fragments of spleen from guineapig or frog dipped in cultures of flagellates of L. tropica had been added. Hawking recently mentioned that numerous forms of L. donovani can be found in tissue cultures made from the spleen of infected hamsters. We obtained pure cultures of L.D. bodies of L. infantum and L. donovani by planting flagellates on tissue cultures.

"In tissue cultures from spleen, plasma and serum from cattle, the flagellates were converted into L.D. bodies within 18 hours. They persisted in the cultures during one month. Subcultures could be made from tissue cultures not older than 22 days.

"Tissue cultures of L.D. bodies from the spleens of hamsters infected with Leishmania were obtained in plasma and serum of rabbits. Subcultures were made from these tissue cultures for up to 15 days.

"Conversion of pure flagellate cultures into L.D. bodies and vice versa could be obtained in vitro by Yacobi's method."

Codounis, A. Leishmaniose et paludisme à évolution simultanée chez un même sujet. [**Leishmaniasis and Malaria developing simultaneously in the same Person.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 1/2, 61–3, 1 fig.

Lowe, J. **Kala-Azar.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 345–6.

In a recent paper by Shortt [this *Bulletin*, 1946, v. 43, 317] Lowe is quoted as saying that urea-stibamine " is as effective as any of the new preparations " ; the author explains that this drug is cheap, fairly safe and effective and is therefore suitable for the treatment of outpatients in India, but has the disadvantage that it must be given intravenously. Some other preparations may be slightly more effective *e.g.* neostibosan, which is not cheap and has not been available for some years, diamidino-stilbene, which is unsuitable because it produces toxic reactions, and " solustibosan " (sodium antimony gluconate), the value of which, however, cannot yet be estimated. " Aminostiburea " is apparently identical with urea-stibamine and is even cheaper, while " stibatin " (Glaxo) appears to be the same as " solustibosan."

The author prefers sternal puncture to splenic puncture and reserves the latter for old-standing cases in which sternal puncture has given negative results. *J. F. Corson.*

Halawany, A. & Jalili, M. **Investigation into the Effect of Penicillin on** *Leishmania Tropica. J. Roy. Egyptian Med. Ass.* 1945, Aug., v. 28, No. 8, 394–6.

" 1. Sodium penicillin in a concentration of 1000 units does not possess any effect on leptomonad forms of *Leishmania tropica* in culture.

" 2. The application of dressings soaked in an aqueous solution of sodium penicillin possessing a strength of 20 Oxford units to each c.c. of distilled water or normal saline, cures the secondary infection but has no effect on the lesion itself. The same can be said of the application of ointment containing 200 units of sodium penicillin in each gram of vaseline."

FEVERS OF THE TYPHUS GROUP.

Fitzpatrick, Florence K. **Studies on Cultivation of Rickettsiae in Eggs.** *J. Lab. & Clin. Med.* 1946, Jan., v. 31, No. 1, 45–55. [37 refs.]

This paper contains a number of useful technical hints in connexion with the cultivation of rickettsiae in yolk sacs ; it should be read by all who are engaged in this work ; only a few examples are given in this summary.

The rickettsial strains employed were the " Breinl epidemic," the " Wilmington murine," and two of " spotted fever " [Rocky Mountain spotted fever].

Eggs from " pullorum tested " flocks of white Leghorn hens were used ; in most cases they were inoculated at the 7-day incubation period. Smears were stained by a modification of the Macchiavello method in which the basic fuchsin was diluted with sterile distilled water which had not been neutralized. Methylene blue was used in staining smears for testing sterility. The fragments of yolk sac used for making smears were taken from the point of attachment to the embryo.

Chick embryos of the 8th or 9th days were found most suitable for inoculation with " spotted fever " rickettsiae. Incubation at 34–35°C. gave the best results with all strains.

With epidemic and " spotted fever " strains, chick embryos were more susceptible than guineapigs to minimum doses of infection ; with endemic strains little difference in susceptibility was observed. Contrary to what happens with viruses, the addition of immune serum to the rickettsial inoculum did not delay the death of the chick embryos.

No antigen was detected in the yolk substance so long as the embryos were still alive, but several hours after death the yolk contained soluble antigen, derived, presumably, from autolysis of the yolk sacs. For experimental study of the antigens it was found better to omit ether treatment of the suspensions, and to add 1·0 per cent. formalin instead of 0·1 per cent. ; the stronger formalin apparently delays the disintegration of the rickettsiae.

John W. D. Megaw.

ZARAFONETIS, C. J. **Serologic Studies in Typhus-Vaccinated Individuals. I. The Effect of a Stimulating Dose of Typhus Vaccine on the Weil-Felix and Complement-fixing Antibodies.** *J. Immunology.* 1945, Nov., v. 51, No. 5, 365–74. [11 refs.]

The author, working with the U.S.A. Typhus Commission in Cairo, studied the Weil-Felix and complement-fixation responses in 100 persons who had previously received standard courses of Cox-type epidemic-typhus vaccine, and in nearly every case two to five later stimulating doses of the vaccine at three-monthly intervals. In every case the last of the stimulating doses had been given at least three months before the first test was carried out. All the sera were tested and immediately a further stimulating dose was given to each person. Later tests were made at intervals of two and eight weeks.

The Weil-Felix titre (*OX19*) was 1–40 to 1–80 in 17 cases just before the stimulating dose ; two weeks later these titres were reached in 21 cases, so that the changes in the reaction were insignificant. The reaction with *OX2* was negative in every case, and only one person gave a positive reaction (1–160) with *OXK*, the titre being the same before and after the stimulating dose ; no explanation could be found for this reaction.

In the complement-fixation tests, both epidemic and murine antigens were used. Before the final stimulating injection, 21 persons were positive with epidemic antigen, and seven of these were also positive with murine antigen. Two weeks after the injection 70 persons were positive with epidemic antigen, and 34 of these were also positive with murine antigen, but usually at considerably lower titres. The findings in 27 cases are shown in a table from which the following analysis has been prepared by the reviewer :—

Complement-Fixation Reactions.

Titres observed	Epidemic Antigen			Murine Antigen		
	Before injection	After 2 weeks	After 8 weeks	Before injection	After 2 weeks	After* 8 weeks
Negative	18	0	13	24	8	17
1–4 to 1–8	7	4	9	3	15	9
1–16 to 1–32	2	19	5	0	4	0
1–64 to 1–128	0	4	0	0	0	0

*In one case no test was made.

From the original table it appears that two weeks after the injection seven persons had titres half as high (1–4 to 1–16) as their epidemic titres (1–8 to 1–32), and eight weeks after the injection two who gave negative epidemic reactions were positive (1–4) with murine antigen ; one other gave the same titre with both antigens, and two had a murine titre half as high as the epidemic titre.

The complement-fixation titres showed a pronounced tendency to return to the pre-injection level within eight weeks of the stimulating dose and the degree of cross-fixation with purified murine antigen " was greater than anticipated."

[The cross-fixation referred to is of interest in connexion with the problem of the relationship between epidemic and murine rickettsiae. Anomalous responses in " endemic-typhus " patients who had previously been inoculated with epidemic vaccine have also been reported by PLOTZ and WERTMAN, this *Bulletin*, 1946, v. 43, 429] and the degree of cross-fixation observed by the author was much greater than that found by BENGTSON [below] for different strains of *Rickettsia orientalis* ; its occurrence may be regarded as favouring the view that *R. prowazeki* and *R. mooseri* are variants of the same species of rickettsia rather than distinct species.

Further investigations will doubtless throw light on these and other puzzling findings obtained in the complement-fixation test as applied to the fevers of the typhus group.] *John W. D. Megaw.*

ZARAFONETIS, C. J. **Serologic Studies in Typhus-Vaccinated Individuals. II. The Effect of Non-Typhus Fevers on the Weil-Felix and Complement-fixing Antibodies.** *J. Immunology*. 1945, Dec., v. 51, No. 6, 375–88.

In this paper the author provides a reply to the important question :— Are typhus-vaccinated persons likely to give rising-titre reactions with the Weil-Felix and complement-fixation tests in attacks of fevers other than typhus ? For all practical purposes the answer is—no !

The present study deals with tests of sera from 104 vaccinated persons suffering from such febrile illnesses as nasopharyngeal catarrh, lobar pneumonia, febricula, atypical pneumonia, and malaria. The amount of vaccine received prior to the illness ranged from three to eight ml. Among the patients 12 gave positive Weil-Felix reactions at titres ranging from 1–40 to 1–160 with *Proteus OX19*, and two reacted at 1–40 to 1–80 with *Pr. OX2*. The titres in every case remained constant throughout the illness, and no positive reactions appeared among patients who were initially negative.

The complement-fixation reaction with epidemic-typhus antigen was positive 1–4 to 1–256 in 55 of the patients ; the usual titres were 1–4 to 1–16. Those who gave positive reactions were tested also with murine antigen and 29 reacted at titres of 1–4 to 1–128. Usually the epidemic titre was twice to four times as high as the murine, but in seven cases the same low titre of 1–4 was observed with both antigens. This relatively slight difference between the epidemic and murine titres corresponded with the results observed by the author in his earlier study of the reaction in vaccinated persons [see abstract above].

The titre rose during the febrile attack in eight cases, but in seven of these the rise was either from 0 to 1–4 or a doubling of the earliest observed titre, and in the one case in which the rise was from 0 to 1–8 the patient had received a " booster " dose of vaccine two days before the onset of the fever. There was, therefore, no evidence of the occurrence of rises in the titre such as occur in attacks of typhus fever.

The high proportion of positive complement-fixation reactions observed in this group is largely explained by the considerable number of the persons who had received " booster " doses of vaccine within the previous two months.

The author points out that with the complement-fixation test a titre as low as 1–4 can be accepted as indicating a positive reaction because no instances of non-specific reactions in properly controlled tests have been reported up to the present time. *John W. D. Megaw.*

RUBIN, S. S. **An Allergic Reaction following Typhus-Fever Vaccine and Yellow-Fever Vaccine due to Egg Yolk Sensitivity.** *J. Allergy.* 1946, Jan., v. 17, No. 1, 21–3.

MOOSER, H. & LÖFFLER, W. Ein Fall sogenannter Brillscher Krankheit in Zürich. Ein Beitrag zur Hypothese der späten Rückfälle beim klassischen Fleckfieber. [**A Case of the So-Called Brill's Disease in Zurich.**] *Schweiz. med. Woch.* 1946, Feb. 23, v. 76, No. 8, 150–53, 1 fig. [17 refs.]

The authors describe a very interesting case of epidemic typhus fever. The patient was an Armenian carpet worker aged 52 years ; he gave a clear history of having suffered from a severe attack of typhus fever in South Russia in 1918. Since his arrival in Switzerland in 1939 he had never been in contact with a known or suspected case of typhus fever, and he had never been infested with lice. The authors state that apart from a few cases of laboratory infection and some isolated cases among refugees who had arrived from Germany during the incubation period, there had been no typhus fever in Switzerland since 1940. The possibility of infection through handling infected articles in the course of the patient's occupation was excluded because imports of all such goods from the east had ceased for several years.

The attack occurred in June 1945 ; it was moderately severe, and lasted 14 days. The rash was pronounced, it extended to the palms and soles and became haemorrhagic.

The Weil-Felix reaction was negative on the 12th day, but was positive, 1–640, on the 19th day, when the complement-fixation test was also positive at a titre of 1–1,280 with epidemic-typhus antigen, and at a titre of 1–320 with murine-typhus antigen.

The authors conclude that the case strengthens the hypothesis of ZINSSER that infection may persist for many years in the body after an attack of typhus fever, and may cause a greatly delayed relapse. This conclusion seems to suggest that the authors incline to the view that infection can be carried over between epidemics by persons who harbour latent infection of this kind, but they emphasize the fact that nothing is known with certainty as to the manner in which infection persists during the inter-epidemic periods. They discuss the other theories dealing with the carry-over of infection and dismiss the view that inapparent infections are responsible ; they consider that the dried-louse-faeces theory is based on the unreliable evidence of what happens in purely artificial conditions. Even the theory of maintenance of infection in rat fleas in the form of murine rickettsiae is admitted to be purely speculative so long as there is no experimental evidence that *Rickettsia mooseri* can undergo transformation into *R. prowazeki*.

No mention is made of an attempt to isolate the rickettsia from the present patient ; the complement-fixation test is accepted as supplying proof that *R. prowazeki* was the causal agent. *John W. D. Megaw.*

BERGER, E. & BRZEZINSKI, S. Chemotherapie der Fleckfieberrickettsien-intoxikation und ihre Aufhebung durch p-Aminobenzoesäure. [**The Chemotherapy of Typhus-Rickettsia Intoxication, and the Inhibitory Effect of p-Aminobenzoic Acid (on the Antidotal Action of Sulphonamides).**] *Schweiz. med. Woch.* 1946, Mar. 2, v. 76, No. 9, 173–4. [17 refs.]

The authors have already shown that the toxic effect produced in white mice by the intraperitoneal injection of lung substance heavily infected with typhus rickettsiae can be greatly diminished by subcutaneous injections of 2 mgm. of sodium sulphathiazole or Na-N-3, 4-dimethylbenzoylsulphanilamide ("Irgafen"). No significant antimicrobic action was observed.

They now show that *p*-aminobenzoic acid inhibits the antitoxic action of the sulphonamides.

All the mice used in the experiments received similar heavy doses of highly toxic rickettsial suspensions, prepared from the pneumonic lungs of infected mice and injected into the peritoneal cavity. The control mice in each set of experiments received these doses and were not otherwise interfered with in any way.

In the first series of experiments three lots of mice were given the standard doses of toxic material, but sodium sulphathiazole had been added 40 minutes before these were administered; all of 10 mice inoculated with this material survived for 48 hours, and also all of 10 mice to which 1·0 mgm. of *p*-aminobenzoic acid had been given subcutaneously in addition. But the third lot of mice, to which larger doses of 10 mgm. of *p*-aminobenzoic were given, had 7 deaths among 10 animals within 24 hours.

There were 15 deaths among 20 control animals within 48 hours.

In the second series of experiments a course of subcutaneous injections of "Irgafen" was started 2½ hours before the injection of the toxic material; five doses of 2 mgm. each were given over a period of 24 hours. Among 12 mice treated in this way there were 3 deaths, all within 16 hours. In another lot of 12 mice treated in the same way, but with the addition of five doses of 2 mgm. each of *p*-aminobenzoic acid, given subcutaneously within five minutes of the doses of "Irgafen," there were 10 deaths within 48 hours.

Of 20 control mice 19 died within 48 hours.

In the third series of experiments *p*-aminobenzoic acid was given by the mouth, in 5 doses of 3 mgm. each, to 11 mice to which the toxic injection was given one hour after starting the same course of "Irgafen" as was employed in the second set of experiments; 10 of these mice died within 48 hours as compared with 5 deaths among 12 mice to which "Irgafen" had been given but to which no *p*-aminobenzoic acid was administered.

Of 20 control mice in this series 16 died within 48 hours.

The authors conclude from these findings that *p*-aminobenzoic acid abolishes the antidotal action of sulphonamides on the rickettsial toxins.

They also discuss the theory that the action of the sulphonamides is on the metabolism of pathogenic organisms, and conclude from their own and other workers' observations that this theory is based on inadequate evidence, and therefore cannot at present be accepted as a working hypothesis in experimental chemotherapy. *John W. D. Megaw.*

Cavaillon, A., Bernard, L., Boyer & Delecourt. La lutte contre le typhus exanthématique en France après la libération. [**The Campaign against Exanthematic Typhus in France after the Liberation.**] *Bull. Acad. Méd.* 1945, v. 129, Nos. 36, 37 & 38, 637–42, 1 fig.

The authors state that typhus fever did not occur in the expected widespread epidemics after the return of about two million persons from Germany in 1945, and explain why this was so.

The first alert was in February when 97 cases occurred among 2,500 Russian soldiers in a camp at Courtine; this epidemic was promptly controlled. A comprehensive plan of action was prepared at a conference of the Ministries, of War, Public Health, and "P.D.R.". A sanitary barrier was set up on the left bank of the Rhine from Switzerland to the North Sea and provision was made for the inspection and disinfestation of every person who crossed the river from the East. Before this had been organized a number of persons had returned to France within the incubation period, so that steps were taken to

ensure the notification and segregation of everyone who had a suspicious febrile attack within 15 days of returning to his home.

The number of cases verified in April 1945, was 31 ; in May it rose to 229 ; in June it fell to 51, and in July to 5. In August, September and October no cases were reported.

The regional public health centres throughout France were supplied with 250 tons of DDT powder [strength not specified].

The Departments specially affected were : the Seine (183 cases, mostly in Paris) ; the Bas-Rhin (20) ; the Rhône (16) ; and the Nord (15). Paris was the main clearing centre to which most of the repatriated converged before returning to their homes.

Three-fourths of the patients were political deportees ; 50 of these came from Buchenwald, 22 from Mauthausen, 10 from Neuengamme, 9 from Dachau, and the rest from 14 other camps.

The success of the campaign was attributed chiefly to dusting with DDT, which was carried out in Germany, on the Rhine, in the Frontier Reception Posts, in Paris, and in the Provinces. The percentage of louse infestation among the patients in the Paris hospitals fell rapidly, from 44 in the middle of April to about 13 in the middle of May. Only 21 secondary cases were detected. Making the fullest allowance for the fact that seasonal climatic conditions were exceptionally unfavourable for the spread of infection from July till October, it seemed certain that disinfestation was remarkably successful. This success was all the more definite because little was done to disinfect clothing or to administer vaccine, though the authors consider that both of these measures ought to have been adopted. *John W. D. Megaw.*

Viel, B. & Romero, H. Dos epidemias de tifus exantematico. [**Two Epidemics of Exanthematic Typhus (in South Chile).**] *Rev. Med. Chile.* 1945, Oct., v. 73, No. 10, 847–54, 2 figs.

The interesting feature of these two epidemics is the striking contrast between the ease with which one of them was controlled by treating all the huts in the affected area with a 10 per cent. DDT powder, and the elaborate organization needed to deal with the earlier one which occurred before DDT was available. *John W. D. Megaw.*

Ecke, R. S., Gilliam, A. G., Snyder, J. C., Yeomans, A., Zarafonetis, C. J. & Murray, E. S. **The Effect of Cox-Type Vaccine on Louse-Borne Typhus Fever. An Account of 61 Cases of naturally occurring Typhus Fever in Patients who had previously received One or More Injections of Cox-Type Vaccine.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 447–62, 1 fig. [26 refs.]

The authors, working with the U.S.A. Typhus Commission, made a careful study of the effects of an ether-extracted Cox-type vaccine in a large group of persons exposed to infection by louse-borne typhus in the course of their work at the Cairo Fever Hospital. The standard of protection aimed at was a course of three doses of vaccine at weekly intervals, followed by single stimulating doses at intervals of 4–6 months. Persons exposed to the same risk, who had refused vaccination, served as controls. Every possible care was taken to avoid the fallacies incidental to observations of this kind. Complete data are recorded in tabular form for 61 patients who contracted typhus after receiving varying numbers of doses of the vaccine ; the only death was in the case of a man aged 35 years who had received a single dose three days before the onset of the illness. The chief findings are shown in the following table :—

Doses of Vaccine	Interval since last dose	Number of patients	Average length of illness (days)	Severity of attack				
				Very mild	Moderate	Severe	Very severe	Fatal
3 or more	21 or more days	26	10½	21	5	0	0	0
2 ...	21 or more days	7	12	4	3	0	0	0
1 ...	21 or more days	11	12·7	2	8	1	0	0
1 ...	Less than 12 days	17	15	4	8	4	0	1
Nil	... ...	10	15½	0	5	2	0	3
Other hospital patients treated at same time, and of same age group.								
No Vaccine		44		1	12	18	5	8

A careful statistical study showed that the disturbing influence of age could be excluded. The findings suggested that administration of the vaccine during the incubation period might lessen the severity of the illness, so that a campaign of vaccination is recommended even during an epidemic. There was no evidence of a falling off in the efficacy of the vaccine up to 325 days after the last dose, but the data do not justify conclusions with regard to the duration of the protection. *John W. D. Megaw.*

MOOSER, Hermann. **Die Beziehungen des murinen Fleckfiebers zum klassischen Fleckfieber.**

This book is reviewed on p. 611.

BOVENTER, K. & FISCHER, R. Ueber das Rattenfleckfieber (endemisches, gutartiges, murines Fleckfieber) in Sizilien. [**Rat Typhus (Endemic, Mild, Murine Typhus) in Sicily.**] *Deut. Tropenmed. Ztschr.* 1944, Jan. 1, v. 48, Nos. 1/2, 1–7.

The authors describe four cases of " rat typhus " seen in Sicily in December 1942, and the first six weeks of 1943. The diagnosis was made on the strength of the symptomatology, the epidemiological conditions of occurrence, and the positive Weil-Felix reaction. Animal-inoculation experiments could not be carried out. Italian observers had already reported the occurrence of 31 cases of the disease in Sicily.

The authors classify the typhus fevers as, louse typhus, rat typhus, tick typhus and mite typhus. They state that the transmitting vectors of rat typhus are the rat and the rat flea. [Presumably they regard the name flea typhus as unsuitable because they accept the view that infection is often acquired through ingestion of food contaminated by the urine or faeces of infected rats ; but even assuming that this view is well founded the more familiar name murine typhus would be preferable.] *John W. D. Megaw.*

PASCALE, H. & CRUZ, E. Considerações sôbre ricketsioses nos municípios de Itapiratiba, São João da Boa Vista e São José do Rio Pardo. (Contribuição ao estudo das Ricketsioses.) [**A Study of the Rickettsial Diseases of the Municipalities of Itapiratiba, São João da Boa Vista, and São José do Rio Pardo (South Brazil).**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1945, June, v. 10, No. 24, 297–304. English summary (5 lines).

The authors have made a diagnosis of flea-borne " Typhus Murinus or Brill's disease " in six cases in São João da Boa Vista in 1944, and in seven cases in

São José do Rio Pardo since 1941. The Weil-Felix reaction (*Proteus OX19*) was positive in high titres and the epidemiological conditions were in keeping with the diagnosis. Tables are given of all the cases in which positive Weil-Felix reactions were observed in both localities since 1939; in the former, four persons gave positive reactions with *Proteus OXK* in 1939 at titres of 1–100 to 1–200, and two other persons reacted with *Pr. OX19* at titres of 1–100 and 1–400 respectively. No other positive reactions occurred till 1944 when all the reactions were of the *OX19* type at titres of 1–1,600 and over. In the latter area during 1939, six positive reactions were observed; they were (1) *OXK* 1–100, (2) *OXK* 1–200, (3) *OXK* 1–800 and *OX19* 1–400, (4) *OXK* and *OX19* 1–1,600 each, (5) *OXK* 1–100 and *OX19* 1–400, (6) *OX19* 1–100. In 1940 the *OX19* reactions greatly predominated, and in the later years no *OXK* reactions have been observed. [This change in the type of the serological findings is curious, it may even give rise to a suspicion that the *Proteus* strains used in the tests were not always true to type.] *John W. D. Megaw.*

Smadel, J. E., Rights, F. L. & Jackson, Elizabeth B. **Studies on Scrub Typhus. I. Soluble Antigen in Tissues and Body Fluids of Infected Mice and Rats.** *J. Exper. Med.* 1946, Feb. 1, v. 83, No. 2, 133–46. [17 refs.]

The studies described in this paper have already been reported in summarized form to the U.S.A. Typhus Commission in August 1944, and March 1945.

Two strains of typhus rickettsiae were studied, "Imphal No. 8" and a Calcutta strain. These had been passed 6–7 times through rabbits and afterwards were maintained by transfer through yolk sacs. Material obtained from yolk sacs of the 12th to 43rd passages was used to inoculate mice and white rats by the intravenous route, and cotton rats by the intracardiac route. The doses given caused death on the 4th to 6th day. Heart blood, pleural fluid, lung and spleen tissues, of the infected animals were used in the experiments for the detection of the antigens; the methods of preparation are described, they included grinding of the tissues and extraction with ether.

Antigens obtained from the tissues of mice infected with one or other strain gave the same complement-fixation responses as sera of mice immunized with either strain, and cross-immunity tests also showed that the strains could not be distinguished from each other.

Antigen prepared from the lung tissues of infected mice was found to be strictly specific when used in complement-fixation tests; the reactions with scrub-typhus sera were positive, those with epidemic and endemic sera were completely negative.

Serum and pleural fluid from mice that had died on the 4th to the 6th day contained the specific antigen, but when the mice had survived for longer periods, as happened after intraperitoneal inoculation, no appreciable amount of antigen could be detected, presumably because of a low rate of production and of the longer time that was available for the formation of neutralizing antibodies.

By high-speed centrifugation of the ether-extracted tissue suspensions it was found that the antigens were present almost exclusively in the "soluble form" in the supernatant fluid; the authors suggest that the antigens had been released because of damage to the rickettsial bodies in the process of grinding and extraction.

Although the sera of the infected animals were much less infective than their tissue suspensions they contained appreciable amounts of complement-fixing antigens, which persisted in undiminished quantity after high-speed centrifugation, and therefore appeared to be in soluble form. Heating the

serum and pleural fluid to 56°C. for half an hour did not destroy the antigens. In ether-extracted tissue suspensions there was a variable rate of diminution of the antigen during storage at 5°C. *John W. D. Megaw.*

Browning, J. S., Raphael, M., Klein, E. F. & Coblenz, A. **Scrub-Typhus.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 481–92, 2 charts. [12 refs.]

This study is based on 173 cases of scrub typhus admitted to hospital from various places in the New Guinea Archipelago. There were six deaths, all of which occurred among 16 patients admitted from one locality within a period of three weeks. Infection was thought to have occurred while they were sitting on the only patch of grass in the neighbourhood.

The Weil-Felix (*OXK*) test was of great value in diagnosis but a titre of 1–80 was seldom reached before the ninth day, and in one group of patients from an isolated area the reaction was uniformly negative.

Some of the chief features of the disease were as follows (figures in brackets are percentages) :—Headache (92) ; orbital pain (62) ; chills or chilly feeling (47) ; eschar (80), usually on the legs or in the axillae ; maculo-papular rash (35) ; and subconjunctival haemorrhage (33). Leucopenia was not frequent but relative lymphocytosis was usual. A pulse rate over 120 per min. usually indicated the presence of a complication.

Among 112 patients examined by electrocardiography about a month after the onset, 16 were abnormal, but 40 per cent. of these became normal within a month.

The chief complications in the acute phase were (in percentages) : impaired hearing (20) ; pulmonary (17) ; abdominal distension (10) ; epistaxis (5) ; arthralgia (4) ; and retinal haemorrhage (2). In convalescence there were seven cases of psychoneurosis and six of " neurocirculatory asthenia," both of these conditions were regarded as due largely to anxiety resulting from reading or hearing reports of permanent damage to the heart. There were four cases of myocardial damage, but the authors believe that there will be no permanent sequelae. *John W. D. Megaw.*

Mendell, T. H. **Scrub Typhus Fever (Tsutsugamushi Disease) in New Guinea. Report of 75 Cases.** *Amer. J. Med. Sci.* 1946, Jan., v. 211, No. 1, 9–22.

This study of scrub typhus is based on 75 cases, of which two were fatal, seen in North New Guinea during the months, August, September and October 1944.

The incubation period was known in only one case, in which it was 21 days.

The area where the infection was contracted consisted of grass and scrub land ; 58 of the cases occurred during the first half of the period, before the site was cleared, and after three months the disease ceased to occur.

The incidence of the chief features was as follows ; figures in brackets are percentages :—The eschar (68) was single except in seven patients, the usual sites were the axilla, scrotum and groin. The macular rash (78) was on the trunk and limbs ; to a " lesser extent " on the face. Adenopathy (95) was most pronounced in the glands associated with the eschar. Splenomegaly occurred in 37 cases. Conjunctivitis (71) affected the palpebral conjunctiva, from which it extended with diminishing severity towards the cornea ; in many cases there were subconjunctival haemorrhages. Deafness (35) was transient except in one case. The central nervous system was specially involved in nearly half the cases. One patient had a severe post-typhus psychosis, with ultimate recovery ; and two others had a temporary psychosis in convalescence,

lasting a few days. Rickettsial pneumonitis or bronchitis occurred in 38 cases (51). Hypotension was a constant feature. Leucopenia was usual, with relative lymphocytosis.

The Weil-Felix test (*OXK*) was carried out in 34 cases ; it was negative in three ; in eight the titre was 1–40 ; and in 23 it was 1–80 or over.

At autopsy in the two fatal cases a vasculitis with perivasculitis was the chief feature ; the vessels chiefly affected were the smaller ones of the brain, lungs, and heart, and the chief changes were in the reticulo-endothelial system.

There was a pronounced tendency to haemorrhages.

Sodium chloride (6 gm. daily) was given as a routine therapeutic measure.

The convalescent period ranged from one to six months. Stress is laid on the need for reassuring the patients to prevent disabling neuroses.

John W. D. Megaw.

Agress, C. M. & Evans, E. R. **Clinical Survey of Eighty-Six Cases of Scrub Typhus.** *Bull. U.S. Army Med. Dept.* 1946, Feb., v. 5, No. 2, 163–9.

The authors studied 86 cases of scrub typhus, of which 79 occurred among Chinese soldiers, in Assam and North Burma, between November 1943 and September 1944. The case-fatality rate was 10 per cent. The average duration of the illness before admission to hospital was seven days. The clinical picture was not unusual in any important respect.

The percentage incidence of some of the chief features was as follows : headache, 86 ; backache, 73 ; cough, 40 ; deafness, 28 ; eschar, 78 ; lymphadenopathy, 94 ; conjunctivitis, 65 ; remittent type of fever, 60 ; intermittent type, 40 ; termination by lysis, 100 ; and positive *Proteus OXK* agglutination, 1–40 or over, 80.

A definite rash was seen in 31 per cent. of the patients, including 10 in whom there was only generalized erythema ; the types of rash observed were : macular, 18 cases ; maculo-papular, 12 ; erythematous, 10 ; and papular, 1. [Presumably in a number of the cases the rash was partly macular and partly maculo-papular.] The rash extended to the face in three cases ; the palms and soles were never affected. There was often a short recrudescence of fever after the temperature had been normal for two or three days.

The leucocyte count ranged from 1,900 to 26,400 per cmm. ; the average count in the 1st week was 9,800 ; in the 3rd week it was 12,100. The percentage of lymphocytes ranged from 9 to 75 ; the average was 29 per cent. in the 1st week, and 43 per cent. in the third.

Among 19 cases tested in the 2nd week the *OXK* reaction was positive (1–25 to 1–1,600) in 11 ; in the 3rd week it was positive in 13 of 18 cases tested ; in the 4th week it was positive in 27 of 30 cases tested ; and in the 5th week it was positive in all the 10 cases tested.

Sulphathiazole was given to 16 patients, but it only added to their discomfort. Plasma, given to 10 patients, caused no striking improvement.

John W. D. Megaw.

Andrew, R. **Fluid Balance in Scrub Typhus.** *Med. J. Australia.* 1945, Dec. 15, v. 2, No. 24, 432–4.

The interesting observations described to this paper are based on a study of 11 severe cases of scrub typhus in North Queensland. The infection in 10 of the patients was contracted on the same day. Sudden diuresis occurred on the 10th -16th day of the disease in 10 of the cases, and on the 32nd day in the remaining case. The average daily fluid intake before diuresis occurred was 97 oz. and the output [presumably urinary] was 44·7 oz. On the first day of

diuresis the average output rose suddenly to 96·4 oz. though the intake had risen by only 20 per cent. to 116·7 oz. The diuresis occurred on the average about three days before the temperature became consistently less than 99°F. and it was accompanied by a striking improvement in the general condition of the patients, though at first sight they looked worse because of the sudden disappearance of the oedema that had masked the pronounced degree of anaemia.

No obvious cause could be found for the diuresis ; in a few cases the blood pressure had been observed before and after the event, but no significant difference was detected, traces of albumin were found in the urine of three patients but there was never anything approaching nephritis. The serum proteins were within normal limits in the cases tested from this point of view.

The findings are regarded as reinforcing the warnings against further deranging the fluid balance in patients with scrub typhus by intravenous injections ; more than five or six pints of liquid daily by the mouth are considered unnecessary.

The climate of the hospital area was hot and humid, the altitude was about 2,000 feet.

[Climatic conditions must be taken into account in estimating a suitable fluid intake.] *John W. D. Megaw.*

Donegan, E. A. **Ocular Findings in Tropical Typhus (Tsutsugamushi or Japanese River Fever).** *Brit. J. Ophthalm.* 1946, Jan., v. 30, No. 1, 11–19.

The eyes of a total of 101 cases of tropical typhus were examined, and the ocular changes may be summarized as follows.—In the acute stage the conjunctivae are generally hyperaemic, without involvement of the cornea, clearing about the 14th day. The fundi typically show a disk in which there is pathological hyperaemia with an overlying central vitreous haze, with its margins blurred in at least two quadrants, often accompanied by swelling. The vessels show little or no change, even in patients with marked cerebral symptoms, as they give no suggestion of venous stasis. The hyperaemia disappears once the acute stage of the disease is over and the fever has subsided. The vitreous haze then clears about the end of the third week. The last sign to disappear is the marginal blurring, which may persist in some cases for more than a month after the substance of systemic signs of the disease. The interpretation placed on the ocular signs is that of a vascular upset, not a neural or neuroglial involvement by invasion of the nerve tissues by the rickettsial bodies. There appears to be only very slight reaction to the organism, which would explain the absence of post-neuritic changes due to fibrosis of the optic nerve and retina. It is not understood why toxic substances which have done so much harm to renal and hepatic tissues should allow the more delicate cells of the brain and retina to escape obvious permanent damage. *E. O'G. Kirwan.*

Irons, E. N. & Armbrust, C. A., Jr. **Relation of the Weil-Felix Reaction to the Clinical Course of Tsutsugamushi Disease.** *Bull. U.S. Army Med. Dept.* 1946, Jan., v. 5, No. 1, 85–94, 8 charts. [16 refs.]

The authors studied the Weil-Felix (*OXK*) response in 74 cases of tsutsugamushi disease, of which seven were fatal. The conclusion is stated as follows—"The incidence of Weil-Felix reaction was inversely proportional to the severity of the illness ; 94·5 per cent. of the moderately severe, 90 per cent. of the severe, but only 29 per cent. of the fatal cases showed a Weil-Felix reaction during the course of the disease." [This conclusion is hardly justified by the facts supplied ; the only significant figure is that relating to the fatal cases,

but the day of death is stated in only two instances, in one of which death occurred on the 15th day and the reaction was positive, while in the other death was on the 16th day and the reaction was negative. Seeing that the delay in the appearance of a positive reaction averaged 17 days, and in some cases was up to 24 days, there is no justification for regarding the negative reactions among the fatal cases as being comparable with those among survivors. Also the classification of the cases as " severe " when the duration of the fever was 18 days or more and as " moderately severe " when it was less than 18 days, irrespective of all other considerations, is open to criticism.

A really valuable feature of the paper is the set of seven charts which show the relationship between the rise and fall of the titres and the course of the illness.] *John W. D. Megaw.*

BENGTSON, Ida A. **Apparent Serological Heterogeneity among Strains of Tsutsugamushi Disease (Scrub Typhus).** *Pub. Health Rep.* Wash. 1945, Dec. 14, v. 60, No. 50, 1483–8.

The complement-fixation titres of sera of animals and human beings infected with different strains of *Rickettsia orientalis* were found to vary greatly according to whether a homologous or heterologous antigen was used in carrying out the test. Most of the experiments described were done with " Karp " (New Guinea) and " Gilliam " (Assam-Burma border) strains. A " Seerangayee " strain (Malaya) was used in some of the tests, it had been found more virulent for guineapigs than the other two strains, whereas the Gilliam strain was the most virulent to chick embryos in yolk-sac cultures. The virulence of an " Imphal " (Assam) strain for chick embryos was exceptionally low, and altogether great differences in virulence were found.

A typical example of the variations in the complement-fixation titres is as follows :—The serum of a guineapig infected by the Gilliam strain gave a titre up to 1–2,048 with Gilliam antigen and up to 1–8 with Karp antigen. So also a Karp-strain serum gave a titre of 1–250 with Karp antigen, of 1–4 with a Gilliam antigen, and of 1–16 with a Seerangayee antigen.

The sera of patients who had been accidentally infected by Karp and Gilliam strains gave correspondingly different responses according to whether a homologous or heterologous antigen was used. In every case the response with the same antigen was at a titre which was at least 100 times greater than that given when the other antigen was used.

The Karp and Gilliam antigens were used in tests of sera from patients suffering from epidemic, endemic, and Rocky-Mountain-spotted-fever infections, and in every case the reaction was negative.

Several groups of serum from cases of tsutsugamushi disease in the Pacific area were tested ; all gave positive fixation against the Karp or Gilliam antigens.

TOPPING has already shown that cross immunity exists between guineapigs that had been infected with the Karp, Gilliam, Seerangayee, and another strain ; it remains to be found whether there is an association between the fixation titre and the degree of immunity. [See the comment on the paper by ZARAFONETIS above.] *John W. D. Megaw.*

CHARTERS, A. D. **Tick-Typhus in Abyssinia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 335–42, 1 chart. [13 refs.]

This is claimed to be the first description of tick-borne typhus in Abyssinia, though the author mentions that the Army Pathological Laboratory Service in its *Current Notes* for December 1941, stated that the disease occurs there, and that the vector is *Rhipicephalus sanguineus*.

Five cases were seen in soldiers at Babile (altitude 5,000 ft.) 17 miles from Harar, within three months, March to June 1943. There was a history of tick bite five to fourteen days before the onset, in three of the first four cases discussed.

A typical *tache noire* was seen in two patients. The fever was irregular ; it lasted for seven to fourteen days. There were slightly raised rose-coloured papules all over the body, including the palms, soles and face.

The percentage of lymphocytes in one case examined on the 9th day was 60 ; in two cases, examined in the first week, it was 39 and 40, respectively.

In one case there was a positive reaction (1–400) with *Proteus OX2* on the 10th day ; in no other patient did the serum react with any *Proteus* strain, but in one case the only test carried out was on the 9th day.

Two patients had unilateral orchitis, commencing 11 and 14 days after defervescence, and lasting a little over a week.

The fifth patient had an afebrile attack, with a typical *tache noire* and a scanty rash. The only symptoms were headache and pain in one shoulder. The patient had been bitten by a tick about a week before the onset. No Weil-Felix test was done.

The tick suspected of being the vector was *Rhipicephalus pulchellus*. Other ixodidae found in the area were, *Amblyomma variegatum*, *A. marmoreum* and *Haemaphysalis leachi*. *John W. D. Megaw.*

BARTONELLOSIS.

MERINO, C. **Penicillin Therapy in Human Bartonellosis (Carrion's Disease).** *J. Lab. & Clin. Med.* 1945, Dec., v. 30, No. 12, 1021–6, 2 figs. [15 refs.]

[A short paper, but of great interest.] Two cases are described in which the use of penicillin seemed to bring about a speedy cure of the infection. The first was in a woman of 21 years who, when admitted to hospital, had been ill with malaise and fever for 23 days. She had been given quinine and atabrine, on a presumptive diagnosis of malaria. She was pale, restless and dyspnoeic. Blood examination gave red cells 780,000, leucocytes 14,970 per cmm., haemoglobin 2·7 gm. per 100 cc. ; percentage differential leucocyte count : myeloblasts 1, myelocytes 9, metamyelocytes 4, neutrophiles 63 (9 of which were *stabkernige*), eosinophiles 3, basophiles 1, large mononuclears 6, lymphocytes 13, and there were many normoblasts [the author states that normoblasts and erythroblasts were present in 61 and 11 per cent., respectively, but does not give his distinctions between the two].

Penicillin was started the day after admission, a total of 300,000 units in doses of 25,000 units every 3 hours, the first four intravenously, the others intramuscularly. In 24 hours the temperature dropped from 39·7°C. to 37·8° and remained down for 4 days, and the general state greatly improved. Fever then returned and rose to 40·4°C. and another 300,000 units of penicillin were given, 20,000 units every 3 hours intramuscularly. Nine hundred cc. of blood were given by transfusion and 2 cc. liver extract intramuscularly. The temperature fell by crisis 10 days later (15th day after admission). Prior to administration of the penicillin 84–94 per cent. of the red cells contained *Bartonella bacilliformis* ; 24 hours after it was started only 20·6 per cent., and on and after the sixth day no cell was found parasitized, even during the secondary rise of temperature. Also, the bacillary forms became generally coccoid, those remaining bacillary had ill-defined borders and were irregularly thickened. The drug did not interfere with erythropoiesis.

The second case was in a man, also of 21 years, who had been ill for 8 days, with headache, chills and irregular fever. He was subicteric, and had a palpable spleen and a few small enlarged but painless glands in the neck and groin ; temperature on admission was 38·2°C. Red cells numbered 4,320,000, white 8,100 per cmm., neutrophiles 59 per cent. (28 per cent. *stabkernige*), eosinophiles 2, large mononuclears 16, lymphocytes 23 per cent. ; 3·4 per cent. of red corpuscles harboured *Bartonella* of the bacillary form. Two days later, red cells had dropped to 3,630,000, leucocytes had risen to 10,850 per cmm., and 31·3 per cent. of the red cells were parasitized. Penicillin, 300,000 units in 20,000 unit doses, was given, the first intravenously, the rest intramuscularly. The fever disappeared in two days and the clinical state improved, and only 6·8 per cent. of the red corpuscles contained *Bartonella*. No more penicillin was available after the two days and the clinical condition deteriorated ; fever returned and 96·5 per cent. of the red cells were seen to be parasitized. Then more penicillin was obtained and 20,000 units were given intramuscularly every 3 hours till 800,000 units had been administered ; after 5 days it was stopped and 2 days later no *Bartonella* were seen in the blood. They had shown the same morphological changes and staining reactions as in the other patient.

It will be interesting to note whether the success in early treatment, the Oroya Fever period, will lead to suppression of the eruptive form, verruga peruviana, later. *H. Harold Scott.*

YELLOW FEVER.

MAEGRAITH, B. **Yellow Fever in West Africa, 1942.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 347–8.

In a paper by ELLIOTT [this *Bulletin*, 1945, v. 42, 276] summaries were given of Maegraith's autopsy reports on two fatal cases of yellow fever in Europeans. In addition to the usual pathological changes seen in yellow fever, there were intensive haemorrhagic lesions in the lungs. These have not often been especially reported, but KLOTZ and BELT [this *Bulletin*, 1931, v. 28, 287] stated that they are found in 90 per cent. of fatal cases. The author briefly describes the kidney lesions in these two cases.

The monkeys inoculated were not *Macacus rhesus* [*Macaca mulatta*] as stated by Elliott but *Cercopithecus nigrifacies* [not mentioned in Allen's Check List of African Mammals, *Bull. Museum of Compar. Zoology, Harvard Coll.*, 1939, v. 83, either as name or synonym].

Another point is that it is very doubtful whether these two patients had been vaccinated with active yellow fever virus as there had been much evasion of inoculation by the troops. Immediately after recognition of the outbreak of yellow fever, reinoculation of the troops was done and no further cases were reported.

The author thinks that Elliott was rather obscure regarding Faget's sign and quotes Faget's words to show that there are really two signs : (1) an initial diagnostic sign—slowing pulse rate and rising temperature ; (2) a final prognostic sign—quickening pulse rate and falling temperature—indicating that death is near [a slight misprint of *on* for *ou* occurs in the quotation].

J. F. Corson.

DENGUE.

PHILIP, C. B. **Infectivity of Dengue Serums transported in Ordinary Ice by Air.** *Bull. U.S. Army Med. Dept.* 1946, Feb., v. 5, No. 2, 226–7.

Dengue virus was isolated in Washington, U.S.A., from four samples of serum collected on the first or second day from patients diagnosed as suffering from dengue or F.U.O. (fever of undetermined origin). The serum had been sent by air from New Guinea packed in wide-mouthed Thermos jugs containing crushed ice which was renewed at each available halting place. The total time of transport was 7½ days. Before despatch the sera had been kept in the refrigerator for 25–26 days in sealed Wassermann tubes.

From two samples of serum, collected at the last minute in corked sterile tubes, a strain of dengue virus was recovered. *John W. D. Megaw.*

PLAGUE.

HAMPTON, B. C. **Plague Infection reported in the United States during 1944 and Summary of Human Cases, 1900–44.** *Pub. Health Rep.* Wash. 1945, Nov. 16, v. 60, No. 46, 1361–5.

The only human case of plague in the United States reported in 1944 was a laboratory infection, in a medical officer of the Public Health Service. This was a case of pneumonic plague, but the patient recovered, and the precautionary measures adopted [which are not described] prevented the occurrence of secondary cases. Since 1900 there have been 504 cases, with 318 deaths.

Information is given on the discovery of plague infection in rodents and their ectoparasites during 1944 ; the names of the rodents concerned are mentioned. The area in which plague was found had extended, the first evidence of infection in Oklahoma being discovered. *Charles Wilcocks.*

HAMPTON, B. C. **Plague Infection reported in the Territory of Hawaii during 1944 and Summary of Human Cases, 1899–1944.** *Pub. Health Rep.* Wash. 1945, Nov. 16, v. 60, No. 46, 1365–8.

During 1944 there were five cases of plague, all fatal, and all from the Hamakua District of the Island of Hawaii. This is an agricultural district, the principal crop being sugar cane, and in recent years more cases have been contracted in the fields than around the houses. The rat most commonly trapped is *Rattus rattus alexandrinus*, and the commonest flea is *Xenopsylla cheopis*. During 1944 plague was found in a considerable number of rodents and pools of their fleas.

Plague was introduced into Honolulu from Hong Kong in 1899, and since then there have been 414 human cases. That the disease is severe is shown by the fact that 377 of the patients died. This disease is now found only in the Hamakua District. *Charles Wilcocks.*

CHOLERA.

LEFROU, G., KERVRAN, P., LOUDOUX, Y. & LE PONCIN, N. La cholérine du Soudan. [**Cholerine of the Sudan.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 11/12, 356–62.

The medical dictionary definition of " Cholerine " is :—" A relatively mild form of Cholera." The organism isolated from the diarrhoeic stools of 5 patients

was, certainly, a vibrio, and these cultures were obtained from some 44 stools in the laboratory of a workers' camp at Bamako in the Sudan during the rainy season. Hospital patients suffering from this comparatively mild intestinal affection, usually curable in two or three days, numbered 351, but probably represented an epidemic affecting some 2,000 persons, with a certain proportion of deaths. Relationship of the vibrio to the cholera group is noted and the authors claim its causal relationship to the epidemic, pointing out at the same time the resemblance of the epidemic to the Cholerine of Senegal or N'Diank, and of the vibrios *Iners*, *N'Dianka* and *enteritidis* of Huri. Attacks of cholerine had no relation to food, were sudden in onset, accompanied by acute colic and frequent aqueous, gelatinous, greenish, but not rice-water, stools. Vomiting was at first watery and then bilious. Other symptoms were cramps, intense thirst and uncertain pyrexia of about 38°C. This vibrio is called vibrio of Bamako, is Gram-negative, has 1 or 2 terminal flagella, is aerobic, grows easily on ordinary media, produces no indole, does not liquefy coagulated serum, does not ferment the usual sugars, does not reduce neutral red nor produce sulphuretted hydrogen, does not haemolyse sheep erythrocytes, is non-pathogenic to guineapig and rabbit and was not agglutinated by patients' serum at 1–100. Treatment was purely symptomatic and ended with administration of a saline purgative.

W. F. Harvey.

CHATTERJEE, H. N. **A Further Biochemical Study of the Blood of Cholera Patients.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 321–6.

This study relates to phenol content (free, total and combined) and reserve alkalinity of the blood of 55 cases of undoubted cholera. It also includes observations on the non-protein nitrogen. A rise in the content of all varieties of phenol has been found, as is illustrated by the averages for normal persons of 2·24 mgm. free phenol, 0·39 mgm. conjugated phenol, and of 2·63 mgm. total phenols, per 100 cc. of blood, with which are contrasted the respective averages of 4·43 mgm. 1·38 mgm. and 5·60 mgm. per 100 cc. of blood for cholera cases examined before saline transfusion. This increase in phenol is real, and is not explained by simple dehydration increase in concentration of the blood, because it has been found in the so-called vasomotor type of cholera, with a low specific gravity of the blood. Against this observation, however, has to be set that of four cases of low phenol content with high specific gravity ; one feature of this small group was that the patients had come to the hospital early and were rapidly convalescent. In the summary it is stated that :—" (1) A markedly high phenol content of blood was observed in all cases of cholera . . . . (2) The specific gravity of blood falls to normal with the transfusions but the increased phenol persisted . . . . (3) Early and comparatively mild cases of cholera . . . showed a rapid return to normal of specific gravity as well as a normal phenol of blood. (4) There was a diminished reserve alkalinity of the blood. This persisted even after the specific gravity and phenol content of blood were brought down to normal. (5) The clinical improvement runs parallel with the improvement of the blood chemistry." *W. F. Harvey.*

CAMPBELL, D. H. & CHERKIN, A. **The Destruction of Pyrogens by Hydrogen Peroxide.** *Science.* 1945, Nov. 23, 535–6.

Pyrogens are toxic, non-dialysable substances formed by various micro-organisms, which cause a rise of temperature when injected into animals. Their true chemical nature is not yet accurately known, but purified preparations exhibit the properties of polysaccharides which can be hydrolysed to

reducing sugars. In the course of an investigation on plasma substitutes one of the authors observed that pyrogenic solutions of gelatin were rendered non-pyrogenic by heating with potassium permanganate or hydrogen peroxide. Further work has shown that if pyrogenic solutions are heated at 100°C. for 60–120 minutes in the presence of 0·1 M hydrogen peroxide their pyrogenic properties are abolished, and at 0·01 M concentration are decreased. The change is not due to alteration of *p*H.

The authors suggest, therefore, that treatment with hydrogen peroxide may be of practical use so long as the hydrogen peroxide does not adversely affect other constituents of the solution, and so long as the amount used is not sufficient to destroy the pyrogens and leave a deleterious excess.

Charles Wilcocks.

BACILLARY DYSENTERY.

Elson, K. A., Pepper, D. S. & Forrester, J. S. **The Treatment of Bacillary Dysentery in Chinese Soldiers with Sulfaguanidine and Sulfadiazine.** *Amer. J. Med. Sci.* 1946, Jan., v. 211, No. 1, 103–9, 3 charts.

From June to December 1943, 334 Chinese soldiers suffering from acute bacillary dysentery were treated in rotation as admitted to a hospital in North Eastern India with (*a*) a placebo, or (*b*) sulphaguanidine 3·5 gm. four hourly, or (*c*) sulphadiazine 3 gm. initially and then 1 gm. four hourly. The diagnosis was clinical; the patients were graded as slightly, moderately or severely ill; stool specimens were examined and bacteriologically cultured early after admission; and a confirmatory bacteriological diagnosis was established in 25 per cent. of the cases, which were found equally distributed in the three treatment groups.

The average periods of fever, of diarrhoea, and of hospitalization were unaffected by the alternative treatments with sulphaguanidine, sulphadiazine, or the placebo; and the authors consider whether this divergent result from the findings of other workers was due to the late stage at which the cases presented themselves (treatment was begun, on the average, 5 days after the onset of symptoms) or to the predominantly mild form of the bacillary dysentery from which most of the patients suffered. They are not convinced that either explanation is the correct one. They observed no toxic effects from sulphaguanidine; but the renal complications from the use of sulphadiazine were frequent and, at times, alarming. Two fatalities might have resulted from the latter but for the available facilities for ureteral lavage, and it is concluded that, under the climatic and other conditions of this study, the dangers of sulphadiazine in the dosage used exceeded those of the disease for which it was given.

A. R. D. Adams.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Rees, C. W. & Reardon, Lucy V. **Comparative Yields of *Endamoeba histolytica*-Organism *t* from Soluble and Insoluble Ingredients of Egg White in Freshly Prepared and Stored Medium.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 109–14. [14 refs.]

Having shown that good growth of *E. histolytica* can be obtained in a modified LES [Locke-egg-serum] medium, in which the whole egg is replaced by egg white enriched with cholesterol and vitamins, the authors attempted to

discover whether the essential ingredient of the egg white was a water-soluble fraction or a heat-coagulable fraction. The egg white was poured into boiling Locke's solution and the coagulum separated by centrifugation. Neither the Locke's solution containing the uncoagulated ingredients nor Locke's solution to which the coagulum had been added were able to replace the Locke's solution and egg white of the modified LES medium. Strangely enough this was also true of the two fractions when combined in a single medium. The operation of separating the two fractions by heat had altered the amoeba-nourishing properties of the egg white. Egg yolk, also, was not a substitute for egg white. In these cultures only a single bacterium (organism *t*) was present and it grew without any difficulty. It was shown that permeable membrane bags containing Locke's solution and organism *t*, when inoculated with *E. histolytica*, allowed growth of the amoebae when the bag was kept in contact with an egg slant overlaid with Locke's solution in which organism *t* was growing. Presumably amoeba-nourishing materials liberated from the egg slant diffused through the membrane in sufficient quantities to permit growth of the amoebae. It was found that though coagulated egg white favoured growth of amoebae when it was confined to the base, this was not the case when it was contained in the overlay.

Another result has been the demonstration that early spring or summer eggs, or pullet egg white, yield a more favourable medium than fall [autumn] or winter eggs. It was found that if medium is stirred it loses its properties if oxygen is absorbed, as through a cotton stopper. If the stopper is rubber and the residual oxygen is absorbed by pyrogallic acid, deterioration of the stored medium does not occur. Under these anaerobic conditions of storage, ovomucoid diffuses from the egg white base into the overlay, with the result that the oxygen-free overlay is capable of yielding a good growth of amoebae. The results appear to indicate that fresh egg white base, acting in conjunction with organism *t*, is concerned in the oxygen potential of the medium. Though the investigation has yielded interesting results, it has not shown what fraction of egg white is responsible for growth of the amoebae. *C. M. Wenyon.*

KERSHAW, W. E. **The Diagnosis of Amoebiasis.** *Brit. Med. J.* 1946, Mar. 2, 305–7.

Amoebiasis is acquired much more commonly by Europeans in the East than is generally realized ; the seriousness of the infection is not fully appreciated there or in the United Kingdom. Of 300 cases, seen in Ceylon, one-half were diagnosed after three and the remainder after eight to twelve stool examinations ; but even this number of examinations cannot be considered as adequate for the detection of every case. Difficulty was experienced in recognizing cysts, which were more readily identified after a modification of Faust's method of concentration had been introduced ; this primarily had the virtue of freeing cysts from the matter which obscured their identification in fresh faecal material. The author considered that there was a regular rhythm in the appearance of amoebae, pre-cystic amoebae and cysts in his cases, both acute and chronic. Sigmoidoscopy was not of great value in the diagnosis of clinically latent cases. *A. R. D. Adams.*

SOKOLOFF, B. **New Aspect in Treatment of Amebiasis.** *Rev. Gastroenterology.* 1945, Nov.–Dec., v. 12, 425. [Summary taken from *J. Amer. Med. Ass.* 1946, Mar. 2, v. 130, No. 9, 607.]

Sokoloff found that lactic acid, even in a weak solution of 1 : 1,000, impedes the multiplication of protozoa, including amebas. Since ingested lactic acid is

actively absorbed in the small intestine and therefore is of little use in the treatment of infections of the large intestine, a special anhydrous form of lactic acid, trilactic, was developed. Trilactic dissolves in water slowly and for this reason reaches the colon and cecum without being affected greatly by the gastric juice. Research has demonstrated that trilactic has a therapeutic effect in animals infected with pathogenic bacteria. Rats infected with Endameba histolytica were submitted to trilactic therapy. Although they had only a mild form of amebiasis, their stools showed presence of trophozoites and cysts. These disappeared after seven days of treatment with trilactic. The animals seemed to have been completely cured. During the last five years trilactic has been tested on a number of patients with amebic infection. In many instances they received the trilactic treatment after emetine had failed to eliminate completely the pathogenic ameba, or when the patient had experienced a toxic reaction from this drug. In a few instances trilactic was administered after protracted iodine therapy when stools still showed presence of the cysts. Such combined therapy showed the most satisfactory results not only in the complete elimination of the ameba but also in the prompt restoration of the normal bowel movement. Sixty-two patients affected with acute and chronic amebic infections have been treated with the anhydrous form of lactic acid known as trilactic. Complete recovery was obtained in 36, improvement in 15 and negative results in 11 patients.

DUNLOP, E. E. **Surgical Treatment of Dysenteric Lesions of the Bowel among Allied Prisoners of War in Burma and Thailand.** *Brit. Med. J.* 1946, Jan. 26, 124–7.

Dysentery levied a heavy toll amongst prisoners of war working on the Thailand-Burma railway. Numerous prisoners suffered simultaneously from dysentery, malaria, tropical ulcer and gross malnutrition, and the medical officers had to contend with shortage or complete absence of specific amoebicidal drugs, lack of facilities for microscopy and for proper nursing and feeding of the patients, and with the action of the Japanese in forcing men with established dysentery to continue working. In consequence many of the patients developed very severe lesions with a tendency to become chronic and emetine-resistant, or to relapse almost immediately on the cessation of treatment. In the acute phase, often with 60 or more motions daily, there was gross cellulitic swelling of the large bowel with tumour formation in the caecal region, sometimes leading to sloughing, perforation and peritonitis. In the chronic cases, scarring, thickening and fibrosis were often found in the caeco-appendicular region at operation. Stricture formation after sloughing was met with principally in the rectum. Drugs, in so far as they were available, had been administered to the patients, in quantities normally curative ; bowel washes of saline, quinine, yatren, silver nitrate, etc, had also been used but had given disappointing results, owing to the intense irritability of the inflamed bowel. The failure of medicinal treatment, and the wretched plight of the patients, led to a trial of surgical measures for the relief of pain and tenesmus. In the more acute cases appendicostomy proved most effective, permitting thorough flushing of the large bowel, whilst in the cases of long standing with a grossly damaged colon, ileostomy was the method of choice, as it afforded complete rest to the large bowel. Appendicostomy was performed in 8 cases, ileostomy in 14, caecostomy in 1, and partial resection of the colon in 3 cases. Three deaths occurred amongst the ileostomy patients, and one after resection of the right half of the colon in a patient who had suffered from an amoebic abscess of the liver, together with a carcinoma of the lip. Six of the eight appendicostomy patients regained good health, with negative stools ; in one case the fistula has been closed and in another

it was allowed to close spontaneously. Seven of the ileostomy cases have regained their health, eating a normal diet and doing light work, and needing only a weekly colon wash-out ; the others are improved. Only one case, so far, has been closed, after two years' rest of the bowel ; in other cases closure was deferred until after evacuation from Thailand. The need for a post-operative course of emetine is stressed, as there is a danger of spread of amoebic infection to the abdominal wall.

[In the same number of the *British Medical Journal* is a paper by Capt. S. S. Pavillard on " Medical Experiences in Siam " (this *Bulletin*, 1946, v. 43, 489) which gives a vivid picture of the terrible conditions under which medical officers had to work in Siam.] *W. L. Harnett.*

Clark, R. H. P. & Dutta, D. K. **Pneumo-Peritoneum in the Investigation of the Right Costo-Hepatic Area.** *Indian Med. Gaz.* 1945, Nov., v. 80, No. 11, 554–6, 6 figs. on 4 pls.

Pneumo-hepatography is a valuable diagnostic aid in determining whether a lesion lies above or below the diaphragm, or whether distortion of a clearly visualized diaphragm is due to deformity of the liver itself. The authors have employed the procedure on 35 occasions without ill effect, except in the case of one elderly patient with a rigid emphysematous chest who suffered pain and dyspnoea for six hours. Emphysema should, therefore, be added to cardiac insufficiency and an acute infection as a contraindication to pneumo-peritoneum.

The methods of inducing pneumo-peritoneum have been reviewed by Maxfield and McIlwain (*Radiology*, 1944, v. 42, 436). Astlett and Jarman (*Lancet*, 1945, v. 1, 304) report fatalities in two cases of pulmonary tuberculosis, one after the 4th and the other after the 14th peritoneal refill. Richards (*Lancet*, 1945, v. 1, 414), commenting on these, adds a record of another fatality due to air embolism on the fourth day after pneumo-peritoneum. Carbon dioxide may be used more safely than air, as it is rapidly absorbed, but on this account the X-ray examination would have to be made immediately after the injection. Maxfield and McIlwain have injected 3,000 cc. or more of this gas into the peritoneal cavity.

The authors give an account of their technique, using a pneumothorax apparatus connected to an 18 or 20-gauge needle. They found 350 to 500 cc. of air sufficient, in Indians of light build, to separate the diaphragm and liver ; and they fluoroscoped the patients in the standing position 4 to 8 hours after its introduction. Both the liver and the spleen may be visualized as the gas accumulates under the diaphragm ; by putting the patient on one side or the other its distribution may be varied.

Notes are given of five illustrative cases where pneumo-hepatography materially assisted in the diagnosis of obscure liver conditions, and reproduction of 14 X-ray pictures illustrates the salient features of these cases. The authors conclude that pneumo-hepatography is a valuable and safe aid to diagnosis.

A. R. D. Adams.

Kark, W. **Hepatic Abscess Secondarily Infected : Penicillin Treatment.** *Indian Med. Gaz.* 1945, Sept., v. 80, No. 9, 451–2.

A British officer, aged 35, was transferred to the author's care on 20th November, 1944, with a history of illness of about one month's duration which had been diagnosed at first as pneumonia and diaphragmatic pleurisy and had been treated with sulphapyridine, 26 gm. in 6 days. Soon afterwards amoebic hepatitis had been diagnosed and ten injections of 1 grain of emetine hydrochloride had been given from 29th October to 7th November. On 30th October the liver margin reached to the level of the umbilicus and X-rays showed

elevation of the right side of the diaphragm ; the patient had irregular fever and his leucocyte count was 17,200 cells, of which 86 per cent. were polymorphonuclears. Sterile fluid was aspirated from the right pleural cavity. Next day, October 31st, thin red fluid containing *Entamoeba histolytica* was aspirated from the upper part of the right lobe of the liver.

By 10th November the " liver " dulness had decreased to the level of the 4th anterior intercostal space above and to three fingerbreadths below the costal margin ; his irregular temperature had " settled " and the leucocyte count was 7,400. On 17th November fever recurred, " liver " dulness reached upwards to the 2nd rib and X-rays showed right pleural effusion ; next day 240 cc. of haemorrhagic fluid were aspirated and 150 cc. on the following day (November 19th).

On transfer to the author's care on 20th November, " liver " dulness extended to the 4th rib and to 1 in. below the level of the umbilicus ; the leucocyte count was 13,200. A second course of 12 injections of emetine hydrochloride was given from 22nd November to 5th December ; his general condition improved and he remained afebrile. On 4th December, 20 cc. of chocolate-coloured pus were aspirated from the right chest ; it contained pus cells but was sterile. The liver dulness now reached to the 7th rib in the mid-axillary line and to three fingerbreadths below the costal margin.

On 7th December he had a rigor, followed by irregular high fever ; no malaria parasites were found in the blood. On 11th December he had severe right shoulder pain ; the leucocyte count was 16,400 with 76 per cent. of polymorphonuclears. Emetine bismuth iodide, 3 grains daily, was given without benefit. On 15th December X-rays showed a large cavity with a fluid level at the 4th rib ; his general condition was grave.

On 18th December two pints of pus were aspirated and 200,000 units of penicillin in 90 cc. of saline were injected into the cavity ; the pus was thick, grey, and very foul-smelling and in cultures showed *Bacterium coli*, *Staphylococcus albus*, and *Bact. alkaligenes*. Sulphathiazole, 6 gm. daily, was given from the 18th to the 25th December, a total of 40 gm. On 20th December the leucocyte count was 20,000. Fever persisted after the course of sulphathiazole and on 26th December X-rays showed a fluid level at the 5th rib ; next day 2½ pints of thick, yellow, sterile pus without foul odour were aspirated and 200,000 units of penicillin in 150 cc. of saline were injected into the cavity. On 28th December the abscess cavity was opened and drained by a de Pezzer catheter ; its capacity was estimated to be 5 pints and about 3 pints of light-yellow, inodorous, sterile pus were evacuated. By 6th January, 1945, the size of the cavity was 6 ounces, and 3 weeks later it was 2 ounces, while after a further 2 weeks there was no discharge and the wound had almost healed.

The author concluded that " either penicillin was the chief sterilizing agent, or the combined effect of the two drugs was a mutually reinforcing one and amounted to more than the sum of the separate actions." *J. F. Corson.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

SERGENT, E. Persistance de *Spirochaeta hispanica* pendant trois ans dans le cerveau d'un cobaye. 3e Note. [**The Persistence of *Spirochaeta hispanica* for Three Years in the Brain of a Guineapig.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Dec., v. 23, No. 4, 245–8, 1 fig.

The author used the same technique as in previous observations on the subject [see this *Bulletin*, 1944, v. 41, 291], and records one example in which

the brain of a guineapig was found to be infective 36 months after spirochaetes had disappeared from the circulating blood. The author's experiments also show that this " Chiffalo " strain of spirochaetes, isolated in 1933, still preserves the same virulence after 313 passages in guineapigs. *E. Hindle.*

Tucker, W. A. L. **A Report on the Treatment of Tick Relapsing Fever with Sodium Penicillin.** *East African Med. J.* 1946, Jan., v. 23, No. 1, 13–18.

The author refers to the marked increase of tick-transmitted relapsing fever (*S. duttoni*) in East Africa, especially in the Western and Buganda Provinces of the Uganda Protectorate, and to the comparatively unsatisfactory results of arsenical treatment in this disease. Accordingly, 36 typical African cases were selected from admissions to hospital, and treated with sodium penicillin. The 36 cases comprised 16 adult males, 9 adult females (4 pregnant) and 11 children. All showed spirochaetes in the blood before treatment was started, and were given doses of 5,000 to 25,000 units of sodium penicillin every four hours, usually intramuscularly but in four cases intravenously. A total dosage of at least 300,000 units seemed to be necessary to effect a cure. For comparison, 19 patients were treated with either neoarsphenamine or sulpharsphenamine.

In the penicillin series the average time for the temperature to return to normal was 23·4 hours, and the blood films became negative in an average of 20·1 hours. The series treated with arsenicals took an average of 16·7 hours for the temperature to return to normal, and 17·4 hours for the blood to become negative.

Three arsenic-resistant cases were treated with penicillin, and all relapsed. Relapse occurred in 27·7 per cent. of all the penicillin cases, and in 31·5 per cent. of those treated with arsenicals.

The author concludes that penicillin does not seem to be more effective than arsenical preparations in the treatment of this strain of relapsing fever, but that penicillin is the drug of choice when jaundice is a prominent symptom. *E. Hindle.*

YAWS.

Ibarra Perez, R. & Gonzalez Prendes, M. A. La frambesia en Bayamo. (Frambuesa, pian, yaws o bubas.) [**Yaws in Bayamo (Cuba).**] *Rev. Sifilografia, Leprologia y Dermatologia.* Marianao, Cuba. 1945, Dec., v. 2, No. 4, 206–18.

Yaws, it is said, was practically unknown in Cuba before Professor Castelló diagnosed it in 1932 in three children of one family in Sagna de Tánamo. Since then the number seen has increased, particularly in the Province of Oriente. Others say that it has been present in Cuba since 1895, introduced from Haiti.

A Commission to study the question was constituted in 1937 and that year 274 cases were diagnosed, 133 of them in Baracoa and 103 in Sagna de Tánamo ; by the following year the total was 1,125, of which 191 were in Baracoa, 111 in Sagna de Tánamo and 567 in Bayamo. In 1941, 99 new cases brought the Bayamo figure to 666, and by 1944 there were 845. It has been generally stated and believed that yaws is largely a disease of the black races, but the authors' investigations go to show that under the same conditions the white races are every bit as susceptible. In fact, of these cases 71·9 per cent. were whites, 19·2 per cent. were half-castes, and only 8·9 per cent. were negroes.

Sex differences were slight, 55·8 per cent. being males and 44·2 per cent. females. The ages were noted in 681 cases; those under 10 years numbered 126 (18·4 per cent.), then in successive decades 249 (36·5), 119 (17·4), 82 (12), 47 (6·9), 40 (5·8) and 12 (1·7); 6 were over 70 years of age. Thus more than half (375 or 55 per cent.) were below 20 years of age. *H. Harold Scott.*

Lopes, C. F. Contribuição ao estudo da lesão primária da bouba. Nota prévia. [**The Primary Lesion in Yaws.**] Reprinted from *Hospital.* Rio de Janeiro. 1945, Dec., 987–97, 9 figs. English summary.

It is generally believed, and is so stated in most, if not all, textbooks that the secondary yaws rash is essentially the same as the primary; in other words, "the secondaries are generalized primaries." The author maintains that there are distinct differences, which any practitioner can recognize. The primary sore is flatter, the secondary heaped up (rupial); the primary is associated with adenitis of the region involved which never goes on to suppuration, and which persists after the sore has healed; the primary sore is very painful, secondaries are accompanied by itching and pricking, but not actual pain. There is another sign, however, of which no mention is to be found in the textbooks, but which is present in one-third of the cases, perhaps more; that is a blanched, squamous, furfuraceous area, 3–5 cm. in extent *to one side* of the primary yaw, not in a circle round it. This is quite different from secondaries which show a peripheral erythematous area, not a blanching. The paper has several photographs showing this quite clearly. Another paper, dealing with the histology of the lesion is promised for the near future.

H. Harold Scott.

da Cunha, A. M. & Guimarães, F. N. Ausência de neurotropismo e viscerotropismo do "Treponema pertenue" no organismo de camondongos inoculados. (Nota prévia.) [**Absence of Neurotropism and of Viscerotropism in Rats inoculated with Yaws.**] *Brasil-Medico.* 1945, Dec. 1, 8 & 15, v. 59, Nos. 48, 49 & 50, 411–13. English summary.

Schlossberger in 1927, following up the work of Kolle and Evers on the production of inapparent syphilis in guineapigs and rabbits, reported that the same occurred after inoculation of the yaws spirochaete [see this *Bulletin*, 1928, v. 25, 659]. The authors have repeated Schlossberger's experiments, but used *Macaca mulatta* [rhesus monkey], because their rabbits died with infection of *Notoëdres cuniculi*, or they might be infected with *T. cuniculi*, which caused, or might cause, confusion with the organism of yaws. Injection of tissue rich in *Treponema pertenue* into eight rhesus monkeys and three Cebidae yielded no result. The authors next inoculated groups of four to eight rats (*camondongos*), 38 in all, with sections of tissue with abundant *T. pertenue*, and at varying periods afterwards killed them, made emulsions of brain, spleen and glands and inoculated human volunteers with the product into scarified areas in the forearm. Half of the rats had shown an ulcer, encrusted over, at the site of their inoculation. The human volunteers exhibited no signs of infection during the ensuing period of observation up to 38 days, but control volunteers inoculated with material direct from the primary case developed typical primary yaws in 2–4 weeks.

The inference from this is that inapparent infection and involvement of brain, glands or spleen, such as occurs in syphilis, does not take place in yaws, and the authors' results do not confirm in any degree the records of Schlossberger. They go further and regard the test as serving to differentiate yaws from syphilis. *H. Harold Scott.*

LEPROSY.

Ibarra Perez, R. & Gonzalez Prendes, M. A. Lepra en Cuba. [**Leprosy in Cuba.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Dec., v. 2, No. 4, 252–72. [29 refs.]

The subject dealt with is comprised in three papers concerned with different aspects of the question. The first, on Leprosy in Havana, is largely historical and epidemiological, and treats of the founding of Havana in 1519, its geographical position and general topography. From available records it would seem that leprosy was known to exist there in the latter part of the sixteenth century, and its introduction is ascribed to colonizers and slaves. In 1681 the San Lázaro Hospital for lepers was founded, the attendants being Sisters of Charity. The town now comprises 43 Wards, and lepers may be found in all; the incidence of leprosy is estimated as 0·47 per mille inhabitants—320 cases among a total population of 676,376. Control is maintained and those who cannot be properly looked after in their homes are segregated; contacts are examined with a view to protecting the healthy public from contamination.

The second paper gives more statistical information on the general prevalence of leprosy in Cuba. The area of the island is given as 114,524 sq. kilometres; 2,539 lepers are registered, and it is thought that the actual figure is round about 4,000. Havana itself has the highest incidence, 5·7 cases per 100 sq. km., Pinar del Rio the lowest, 0·48. Taking the figure of 4,000 as fairly correct, the incidence of leprosy in Cuba would be, on an average, 3·49 per 100 sq. km.

The third contribution deals with the incidence of leprosy in Cuba relative to the population. In this paper the authors revert to the figure of 2,539 *known* cases, previously given, which, with a population of four and three-quarter millions, gives a rate of 5·3 per 10,000. Of the total cases, 592 are in hospitals and 1,947 free to move about. In the provinces of Camagüey and Oriente, the proportion of ambulant cases is 5·15 per 10,000; Havana has 3·82, and Pinar del Rio fewest, with 1·66. After giving the above figures the authors reiterate the statement of the preceding paper that the probable number of lepers in Cuba is about 4,000. *H. Harold Scott.*

de Castro Palomino, J. & Alfonso y Armenteros, J. La lepra en el dispensario Saenz. Estadistica de los casos atendidos durante dos años. [**Statistics of Lepers attended at the Saenz Dispensary (Cuba) 1943–45.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Dec., v. 2, No. 4, 249–51.

Altogether 119 new cases have been seen in the 2-year period. Sixty were males, 59 were females. As regards type of disease, 65 were lepromatous, 22 tuberculoid, 12 " non-characteristic " and 20 " unclassified". It has been the rule to examine them all bacteriologically, to make histological and biological investigations and to estimate the blood sedimentation rates. Seventeen have been transferred to other dispensaries, leaving 102, of whom 3 have died and 30 have disappeared and cannot be traced. As regards race, 96 were whites, 6 negroes, 16 half-castes, and one a Chinese. Two were under 10 years old, 10 were in the second decade, and in succeeding decades to the seventh the figures were 24, 34, 22, 12 and 12; there were three patients over 70 years of age. *H. Harold Scott.*

Pereira, P. C. R. As leprolinas Souza Araujo—seu emprego—resultados em comparação com a reação de Mitsuda. [**Tests with Souza-Araujo Leprolins compared with Reactions to Mitsuda's Lepromin.**] *Mem. Inst. Oswaldo Cruz.* 1945, v. 42, No. 1, 217–21.

The author has tested the leprolins of Professor de Souza-Araujo [see this *Bulletin*, 1945, v. 42, 1010–12] in two groups of lepers, one (28 in number) no longer harbouring the bacilli, the other (29) with bacilli, and has compared the results with those obtained from Mitsuda's lepromin. Positive reactions were evidenced by erythema of varying extent, lasting for a few days and then gradually fading; rarely the erythema would appear late, some 8–12 days after injection of the antigen. Nodules varying in hardness with tissue reaction might also appear and occasionally there was suppuration with loss of tissue. In both groups three failed to give any reaction to the leprolins. In the first group, the non-bacilliferous, 15 reacted to all the antigens and all 25 to antigen 4. In the second (bacilliferous) group one only reacted to all four antigens, but all the 26 did so to antigen 4.

As regards Mitsuda's lepromin reaction, this was tested in the nonbacilliferous group only. A table gives the results in each of the 28 patients. These may be summed up by saying that they were not in accord; a patient might give a positive to leprolin but negative to lepromin.

H. Harold Scott.

Chorine, V. Traitement des lésions oculaires de la lèpre. [**Treatment of the Ocular Lesions of Leprosy.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 255–71. [21 refs.]

The treatment of the ocular complications of leprosy is discussed by Chorine. He points out that the eyes are frequently attacked by the disease, but that the statistics collected by workers in different countries are contradictory. As examples of these he quotes the figures of Rogers and Muir [this *Bulletin*, 1925, v. 22, 256] for India at 5 to 10 per cent., those of Pinkerton (*Arch. Ophthalmology*, 1927, v. 56, 42) in Hawaii and of Jeanselme [this *Bulletin*, 1934, v. 31, 754] in Indo-China at 100 per cent., those of Fedoseev and of Pavlov in Soviet Russia at 62 per cent. It is the opinion of most authorities that the longer the duration of the disease, the commoner the ocular complications; that the nodular type more frequently causes involvement of the eyes than the neural type and that ocular complications of leprosy, including blindness, are much less frequent in warm than in temperate and cold climates.

The author advocates the use of sulphonamides parenterally and recommends the following solution :—

Acetamide	60 gm.
Septoplix [sulphanilamide]	15 gm.
Distilled water	100 cc.

The injections are painful and are given around the circumference of the orbit. A preliminary injection of 4–5 cc. of 1–2 per cent. Stovaine is given into the orbit, and then the sulphonamide solution is injected into the anaesthetized area. Both eyes are treated simultaneously and one or two injections of 2 to 5 cc. are given into each orbit. Small doses are given at first to test the reaction of the patient, and the injections are carried out once a week. The author reports remarkable improvements in the ocular complications as a result of this treatment.

E. O'G. Kirwan.

Pereira, O. de Loiola. **Contribuição ao Estudo do Tratamento da Lepra segundo os resultados obtidos em 10 anos de Terapêutica Antileprótica na Leprosaria Central de Gôa.**

This book is reviewed on p. 609.

HELMINTHIASIS.

Vishnievskaya, S. M. [**Helminthological Examination of Sewage, Soil and Vegetables from the Bezludov Fields Manured with Sewage.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 4, 14–18. [In Russian.]

After quoting several Russian papers on the contamination of vegetables by helminth eggs, the author records his examination of sewage water from the main and secondary canals used to irrigate the Bezludov fields and also of the sediment from these. He also examined washings from vegetables (tomatoes, cucumbers and cabbages) grown on these fields. The observations were made in 1937 and 1938. Water samples were taken from the canals in bottles containing 48 litres ; these stood for two days before the sediment was examined by the author's modification of the method of Lein [no reference to this method is given]. Soil was taken from the surface of both irrigated and non-irrigated areas, and also at a depth of 12 cm., in samples of 200 to 250 gm. Vegetables were washed twice and both washings were centrifuged, the sediment after centrifugation being examined by the method of Lein.

The author found in the sewage water from the irrigation canals eggs of those species of helminths which have been found in the impure sewage water of the Kharkov district, namely, *Ascaris*, *Trichuris*, *Trichostrongylidae* and a cestode referred to as "the dwarf-chain" [some other Russian authors mean by this phrase *Hymenolepis nana*, but, unless the Latin name is given, it is difficult to be sure what species is meant]. The majority of the eggs found were those of *Ascaris* and the following figures refer to these only. More eggs were found in 1 litre of the water from the main canals, *i.e.* 22–40 per litre, than in the same amount of water from the secondary canals, *i.e.* 14–18 per litre. The author claims that this fact demonstrates the part played in " dehelminthization " by the canals. In the sediment from the main canals there were 3 to 10 eggs per gm. and in the soil from the irrigated areas there were only 0·5 to 1 egg per gm. Thus the passage of the water along the canals at a speed of 22 cm. per second removes, the author claims, 50 per cent. of the eggs. The eggs of *Ascaris* found were not usually morphologically altered ; they were segmenting and, under favourable conditions, most of them developed until infective larvae were formed in them. In the surface layer of the soil of the irrigated areas, up to 70 per cent. of the eggs of *Ascaris* were morphologically unchanged, and 23 to 30 per cent. of them were deformed. Isolated eggs, when they were incubated, developed until they contained infective larvae. In ploughed soil of the irrigated areas the author found that from 65 per cent. (in 1937) to 80 per cent. (in 1938) of the eggs were morphologically unchanged, and these developed under favourable conditions until they contained infective larvae. In soil from the irrigated areas taken at a depth of 12 cm., 55 per cent. of the eggs of *Ascaris* were morphologically unchanged, but these did not develop under favourable conditions. In the soil from areas irrigated only before they were ploughed, isolated eggs of *Ascaris* were found whose external appearance suggested that they were morphologically unchanged.

In sediments obtained after washing vegetables grown on the Bezludov fields the author found an average of 0·3 to 1 *Ascaris* egg per gm. of sediment.

Isolated eggs of *Ascaris* were found on the vegetables grown on fields irrigated with sewage during the summer ; but no eggs of any helminth were found on vegetables grown on land irrigated with sewage water during the autumn or winter ; nor were any eggs found on vegetables from areas irrigated only before they were ploughed. [*Cf.* VASILKOVA, this *Bulletin*, 1945, v. 42, 569.]

G. Lapage.

ALF, S. [**Contamination of Soil by the Eggs of Helminths by the Burial of Sewage.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 4, 18–22. [20 refs.] [In Russian.]

After reviewing the literature on this subject the author records his observations on three shallow pits, each with a capacity of 1 to 1·25 cubic metres, in which faecal matter was buried. Two pits were in sandy soil and the third was in clay soil. The faeces contained 1,000 to 2,000 eggs per gm. and in 65 per cent. of these eggs active embryos developed under favourable laboratory conditions. These 65 per cent. were eggs of *Ascaris*. [The author does not state whether eggs of other species were found.] Samples of soil were taken with a soil borer around each pit at horizontal distances of 0·5, 1, 2 and 3 metres from the walls of the pits and at vertical depths from the bottoms of the pits of 0·5, 1·25 and 2·5 metres. These samples were taken in different directions at right angles to each other. Similar samples were taken from control plots distant 9 metres from pit no. 3 and 5 metres from pit no. 2. Each sample consisted of not less than 1 kgm. of soil. The eggs were recovered from the samples by a modification of the method of SPINDLER [no reference to this method is given], samples of 300 gm. of soil being thus examined. The results showed that there was no infection of the soil at horizontal distances of 0·5 to 3 metres from the walls of the pits, or at vertical depths from the bottoms of the pits of 2·5 metres (*i.e.* 1 to 1·25 metres below the bottoms of the pits).

G. Lapage.

COCKBURN, C. **Ocular Cysticercus Cellulosae. Report of a Case of Parasite in Vitreous.** *Brit. J. Ophthalm.* 1946, Feb., v. 30, No. 2, 65–74, 5 figs. (1 a coloured pl.).

COLE, G. **Hydatid Disease in Victoria.** *Health Bull.* Melbourne. 1945, Jan.–June, Nos. 81–82, 2178–88, 1 map. Addendum I, II & III, pp. 2189–92, 2 figs.

Hydatid disease was made notifiable in Victoria in 1926 and from then to the end of 1944, 278 cases have been notified, 136 of them in the Western Health area, 52 in the Central, and 48 in the North-western areas. That is, 44·6 per cent. of notified cases have occurred in an area less than one-eighth of the State, with 4·4 per cent. of the State population ; it is practically certain that several escaped notification. The disease is, in the main, restricted to the sheep-country, and investigations at various abattoirs showed that from 28·7 to 71 per cent. of the sheep killed were infested with hydatids. Also, of 24 dogs whose faeces were examined, 6 were passing adult *Echinococcus granulosus* ; these animals are commonly fed with uncooked offal from the slaughterhouses. Preventive measures are simple, easily understood and easily applied, and a vigorous campaign is suggested : the appointment of a committee to investigate the problem more deeply, and the adoption of a publicity campaign ; the preparation of a wall-sheet showing the life-history of the worm, and the distribution of it to all schools ; exhibiting posters of similar design in abattoirs and at railway stations ; the wide distribution of leaflets, and securing publicity by Press co-operation. The article mentions five other cestodes which may

infest dogs, namely, *T. hydatigena* (intermediate *Cysticercus tenuicollis*), *T. pisiformis* (*Cysticercus pisiformis*), *T. serialis* (*Coenurus serialis*), *T. ovis* (*Cysticercus ovis*) and *Dipylidium caninum*, the last only infesting man.

There are three addenda to the main article; the first gives details of the investigation of dogs referred to above; the other two are pamphlets of general information issued by the Medical Officer of Health and the Commission of Public Health. The last contains an excellent illustration of the small intestine of a dog heavily infested with the cestode. *H. Harold Scott.*

Lasnier, E. P. & Cassinelli, J. F. Diagnóstico de quiste hidático hialino (no roto) del pulmón mediante la inclusión de esputos. [**Diagnosis of Unruptured Hydatid Cyst of the Lung by Examination of the Sputum.**] *An. Facul. de Med. Montevideo.* 1945, v. 30, No. 12, 903–45, 14 text figs. & 5 coloured figs. on 1 pl. [32 refs.]

This long article pleads for examination of the sputum in patients with unruptured hydatid cyst of the lung. The authors show, with illustrative photomicrographs and a coloured plate, how by suitable staining (particularly by Best's haematin and carmine method) fragments of the cyst-wall and minute cocco-bacillary bodies can be seen and diagnosis made. All this is gone into in much detail, for which those interested must consult the original. *H. Harold Scott.*

Hunter, G. W., III & Worth, C. B. **Variations in response to Filariform Larvae of *Ancylostoma caninum* in the Skin of Man.** *J. Parasitology.* 1945, Dec., v. 31, No. 6, 366–72, 1 fig. [16 refs.]

Reports of the effects of penetration of the human skin by filariform larvae of *Ancylostoma caninum* have varied; some record a transient papular dermatitis, others deeper penetration and creeping eruption.

Two volunteers submitted themselves to infection on the right forearm with 1,000 or more filariform larvae of *A. caninum*. In both cases the immediate reaction was acutely inflammatory; after that their reactions differed sufficiently to warrant separate description.

The first volunteer felt an itching, and the area in 45 minutes became erythematous; in 48 hours urticaria and papules were numerous and on the third day induration and tenderness, and sulphadiazine was prescribed. Except for a slight rise of temperature, less than 1°F., on the 2nd and 3rd days, there was no systemic disturbance. Subsequently, at intervals increasing in length, there occurred attacks of transient urticaria. Biopsy revealed no parasites, and the stools, examined up to 180 days after infestation, remained negative for ova. Leucocytes on the 3rd day totalled 9,900 per cmm., with eosinophiles 2 per cent.; the highest eosinophilia was 9 per cent. among 8,850 leucocytes on the 85th day.

The second volunteer had an allergic history, personal and familial. His immediate reaction to the application of the larvae was less intense; on the 3rd day there was spreading inflammation with some superficial tenderness, and papules were becoming vesicular. Burrows were visible on the 4th day. On the 7th there was deep induration of the forearm, with aching pain and pitting oedema. Several times during the ensuing months there were renewed burrowings and localized swellings. But, whereas with *A. brasiliense* the burrows are continuous with the site of entry of the larvae, *i.e.* the larvae possess "invasive properties against a poorly resistant host," in the case of *A. caninum*, there is local arrest and the larvae penetrate deeper and rise to the surface again at a distance (in the case of this experimental subject, some

7–8 in. from the site of entry). No ova were seen in the faeces at any time. In this volunteer the blood showed an eosinophilia of 26 per cent. on the 29th day, in a total leucocyte count of 12,800, and of 15 per cent. on the 72nd day in a total of 12,000, after which the eosinophilia fell till the 181st day, when the number rose to 1,072 (or 8 per cent. of a total leucocytosis of 13,400) from 522 (6 per cent. of 8,700) on the 120th day. It may be concluded that " the human subject [may] vary constitutionally in his ability to arrest the invasion of a parasite which may be considered uniform within its species."

H. Harold Scott.

MILWIDSKY, H. **The Surgical Complications of Ascariasis.** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*). 1945, Nov., v. 4, No. 11, 370–84. [28 refs.]

An account of the surgical complications of ascariasis, illustrated by clinical details of 17 cases met with during six years' surgical practice in Jerusalem. The most common complication is intestinal obstruction, of which there are four varieties, (1) mechanical, (2) spastic, (3) intussusception, (4) volvulus. Five cases of mechanical obstruction, all submitted to operation, are recorded ; two early cases, in which the bowel was not opened, recovered and three with gangrenous intestine and peritonitis ended fatally after resection of intestine or ileostomy. Two cases are described in which the obstruction was due to ileus, in one of these the symptoms passed off after the administration of a spinal anaesthetic, the other proved fatal after laparotomy and ileostomy. Intussusception and volvulus of the lower ileum occasionally occur. Three patients with the latter condition were operated on, two of whom recovered, in one case after resection of 30 cm. of gangrenous gut and a temporary ileostomy. The mortality of this group of 10 cases was 50 per cent., cases which recovered being those in which the symptoms were of only one to two days' duration.

Perforation of the bowel may take place through areas of inflammation or ulceration, or through suture lines postoperatively. A case of persistent duodenal fistula after gastrectomy for duodenal ulcer is described, in which an *Ascaris* was eventually expelled through the fistula, with subsequent healing of the wound. Appendicitis may, of course, occur in infested subjects, but cases are met with in which it appears to be directly due to the irritation caused by the parasite entering the appendix ; two such cases are cited, both of which recovered after appendicectomy.

Acute abdominal symptoms suggesting perforation of a duodenal ulcer may be caused, and two patients sent to hospital with this diagnosis were spared operation, because in one case vomiting of some worms led to immediate improvement and in the other the fact that the patient had had two similar attacks during the previous 18 months, for the first of which a laparotomy had been performed and only *Ascaris* infestation found, suggested the true diagnosis.

The bile and pancreatic ducts may be blocked by the worm migrating up the common bile duct, setting up cholangitis, cholecystitis and abscess of the liver, all of which have been recorded. One of the author's cases arrived in hospital with a diagnosis of empyema of the gall-bladder, but here too the vomiting of worms led to investigation and a correct diagnosis.

The differential diagnosis is discussed, but stress is laid on the imperative necessity of surgical intervention in the presence of acute abdominal symptoms and signs, without waiting to see the effects of anthelmintic treatment. If a non-urgent abdominal operation has to be performed in an *Ascaris*-carrier, pre-operative anthelmintic treatment is advisable. *W. L. Harnett.*

ALEXANDER, A. E. & TRIM, A. R. **The Biological Activity of Phenolic Compounds. The Effect of Surface Active Substances upon the Penetration of Hexyl Resorcinol into** *Ascaris lumbricoides* **var.** *suis*. *Proc. Roy. Soc.* Ser. B. 1946, Feb. 12, v. 133, No. 871, 220-34, 7 figs. [27 refs.]

This paper must be read in original if it is to be fully appreciated.

The authors have devised a method of measuring quantitatively the effect of surface-active substances (sodium cholate, sodium oleate and cetyl trimethyl ammonium bromide (C.T.A.B.)) upon the penetration of hexylresorcinol into the nematode, *Ascaris lumbricoides*, parasitic in pigs. Parallel measurements have been carried out on the interfacial activity of solutions of the substances named against an inert mineral oil, "Nujol", which is a pure high-boiling paraffin. The work should be read in conjunction with the work of TRIM [this *Bulletin*, 1944, v. 41, 596], ROGERS [*ibid.*, 1945, v. 42, 299] and the other authors quoted.

The action of all three substances was markedly similar and differed only in degree. When a fixed concentration of hexylresorcinol was used (0·025 per cent.), the soap in dilute solution accelerated the penetration of the drug, the maximum acceleration being in the order sodium cholate ≪ soldium oleate < C.T.A.B. High concentrations of the soaps, however, completely inhibited the penetration of hexylresorcinol. The soaps alone penetrated *Ascaris* only very slowly, if at all. The soap and the hexylresorcinol molecules associate at an interface, forming a labile complex of increased surface activity. The authors suggest that the biological activity of hexylresorcinol, as measured by its rate of penetration of the cuticle of *Ascaris*, is determined by the interfacial activity of this mixture, and that, when soap micelles are present, the drug distributes itself between the micelles and any other interface present, such as oil/water or *Ascaris*/water. Thus the maximum biological activity occurs at the critical concentration for micelle formation, because this has maximum interfacial activity. At high soap concentrations the hexylresorcinol is held mainly by the soap micelles, so that the biological activity is diminished; ultimately it is diminished to zero, because the soaps alone penetrate so extremely slowly. It has been possible to calculate, from the data provided by the use of C.T.A.B./hexylresorcinol mixtures, a theoretical curve for the biological activity of hexylresorcinol which agrees well with the results of experiment. The authors discuss the possible bearings of these results upon the anthelmintic activity of hexylresorcinol *in vivo* and also upon the action of drugs in general (*e.g.* the action of soaps together with phenols upon bacteria). The authors say that it may be "quite feasible, by adjustment of the relative amounts of drug and soap, to control not only the intensity of biological activity but also the duration at any desired level up to the optimum. With drugs that have undesirable effects on the host, this clearly is of great value."

G. Lapage.

HARRIS, J. S. & SUMMERS, W. A. **A Concentration Method for demonstrating Microfilariae in Blood.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 497–8.

Four cc. of blood are taken from a vein and put into a tube containing 0·01 cc. of heparin solution ("Liquemin Roche-Organon Inc. 1 ml. contains 10 mgm. of purified heparin"); 4 cc. of a 2 per cent. aqueous solution of saponin are added and mixed with the blood. When haemolysis is complete, 6 cc. of the mixture are centrifuged for 10 minutes at 2,000 r.p.m. The supernatant fluid is drawn off, leaving 0·1 cc. in the tube and this is spread on a slide and examined with a low power of the microscope; if desired it can be stained afterwards.

The authors found this method superior to other concentration methods.

J. F. Corson.

Augustine, D. L. & Lherisson, C. **Studies on the Specificity of Intradermal Tests in the Diagnosis of Filariasis.** *Amer. J. Hyg.* 1946, Jan., v. 43, No. 1, 38–40.

Earlier work has suggested that intradermal tests done with antigen derived from *Dirofilaria immitis* of the dog has value for diagnosis of filariasis of man. The authors quote, for example, Taliaferro and Hoffman [this *Bulletin*, 1931, v. 28, 214], Fairley [*ibid.*, 1932, v. 29, 427], Dickson, Huntington and Eichhold [*ibid.*, 1944, v. 41, 303], Michael [*ibid.*, 956]. But later work by Wright and Murdock [*ibid.*, 1054] and Huntington (*U.S. Nav. Med. Bull.*, 1945, v. 44, 707) has given irregular and uncertain results. [See also Zarrow and Rifkin, below.] Positive reactions, ascribed to cross reaction with other nematodes, especially intestinal species, have been obtained in a large percentage of subjects who showed no clinical symptoms of filariasis; and negative reactions, ascribed to desensitization, have been obtained in persons with acute, severe symptoms of Bancroftian filariasis. The authors thought that this lack of specificity of the test might be due to sensitization by repeated exposures to species of filariid nematodes which do not infest man. Adult filariid nematodes are common in frogs, lizards, birds and mammals. These adults are markedly host-specific and there are as many (or more) species of filariid nematodes as there are species of land vertebrates. It is very likely that filariid nematodes are the commonest helminth parasites of land vertebrates in regions where *Wuchereria bancrofti* is endemic.

The microfilarial larvae of these species, however, are less specific to their intermediate hosts. They can develop in many arthropods, especially in mosquitoes. The life-histories of the species not parasitic in man have not yet been worked out. We can expect that they follow the usual pattern shown by *Dirofilaria immitis* of the dog. The microfilarial larvae of *D. immitis* can develop in more than 20 species of mosquitoes belonging to three genera. Its possible intermediate hosts include the usual vectors of *W. bancrofti* and of human malaria. " Effective transportation to man of infective larvae of non-human filariae seems unquestionable, and, in all probability, this is a very frequent occurrence." It is also very probable that these microfilarial larvae which enter man are destroyed in his skin, as the infective larvae of the hookworms of dogs and cats, and the cercarial larvae of avian and rodent schistosomes, are. But repeated infestations of man with these microfilarial larvae can be expected to provoke a potent " immune reaction".

The authors therefore studied the specificity of skin tests done on rabbits with antigens made from filariid nematodes which are not parasitic in man, namely, *Dirofilaria immitis* of the dog, *Setaria equina* of the horse, *Litosomoides carinii* of the cotton rat and *Vagrifilaria columbigallinae* of the ground dove. Adult nematodes of these species were washed in running water and then given several baths of distilled water, before they were dried over sulphuric acid *in vacuo* for 2 to 3 days. The dried nematodes were ground up and extracted for 3 days in physiological saline containing 1 : 10,000 merthiolate. After centrifugation, the supernatant fluid was used as antigen. Dilutions were made on a dry-weight basis and all tests were done on rabbits about 1 year old.

Each of four rabbits was first immunized by subcutaneous injections, on eight occasions, of 1 cc. of antigen diluted 1 : 1,000. On the tenth day after the last injection the intradermal tests were done by injection into a hairless region of the skin of the back of 0·2 cc. of antigen. Control tests were done with physiological saline containing merthiolate. All the antigens were also tested on normal rabbits. A reaction was considered positive when the diameter of the weal produced by the antigen exceeded that produced by the saline, by 3 mm. or more.

The four immunized rabbits were all positive to dilutions of 1 : 1,000 and 1 : 8,000 of each of the antigens. The tests done with the 1 : 1,000 dilutions were the first to appear and the last to fade ; they were more prominent and were positive 2 hours after the injections. " By this time the weals caused by both specific and the non-specific antigens varied from 30 millimeters in diameter to 50 by 70 millimeters for antigens in a dilution of 1 in 1,000." The largest weals were produced by the *D. immitis* antigen in a rabbit immunized with antigen from *V. columbigallinae* of the ground dove. This weal disappeared 18 hours after the injection, as did also the weal produced by *Setaria equina* antigen ; the reaction produced by the specific antigen from *Litosomoides carinii* of the cottonrat was, however, still present at this time. Dilutions of 1 : 8,000 of the antigens produced milder reactions. After 2 hours the weals had a diameter of 15 to 30 mm. and after 18 hours they were not conspicuous. The authors say " there was no marked erythema or oedema, except in all the tests with *Dirofilaria immitis* antigen in 1-in-1,000 dilution. Erythema and oedema were particularly prominent in the specific tests." All the reactions were inconspicuous or had disappeared after 18 to 30 hours. All the controls were negative. The duration of the sensitivity was not determined. The authors state that their experiments afford no direct evidence that infestations with the microfilarial larvae of filariids not parasitic in man can produce sensitivity in man, but claim that their work shows clearly that the extracts of the filariid species used caused an immune response, indicated by skin tests, whether the antigen was specific or not. They therefore feel " justified in supposing " that (*a*) non-human filariid nematodes can influence the serological reactions of man, and (*b*) many hitherto unexplained false positive skin reactions to *D. immitis* antigen are due to responses produced by filariid nematodes which are not parasitic in man. *G. Lapage.*

ZARROW, M. & RIFKIN, H. **Observations on the Specificity and Clinical Use of *Dirofilaria immitis* Antigen in the Diagnosis of Human Filariasis** (*Wuchereria bancrofti*). *Amer. J. Med. Sci.* 1946, Jan., v. 211, No. 1, 97–102. [18 refs.]

Reviewing the literature on this subject, the authors recall that KING [this *Bulletin*, 1945, v. 42, 304], suggested the following three methods for the diagnosis of filariasis :—(1) Microscopical demonstration of adult filariae by means of biopsy. The present authors agree that this method is certain, but it takes time, involves surgical removal of lymph nodes and perhaps the removal of several of these if the first ones removed are negative [see below] and it is not applicable to a field survey. (2) Demonstration of microfilariae in the peripheral blood. To this method the present authors object that nobody has yet demonstrated microfilariae in the blood of United States soldiers, although they are abundantly present in the blood of natives of the areas investigated. In the present study, moreover, no microfilariae were found in the blood of the white subjects studied, although repeated examinations were made both of fresh smears and by the concentration method of KNOTT [this *Bulletin*, 1940, v. 37, 304]. (3) Demonstration of calcified filarial nematodes by Roentgen ray techniques [see O'CONNOR, this *Bulletin*, 1930, v. 27, 986]. The present authors state that it has not yet been shown that these techniques have any diagnostic value. They therefore decided to use a skin test.

A review is given of the literature up to 1944 on intradermal tests with antigen derived from *Dirofilaria immitis*, *Wuchereria bancrofti* and *Litosomoides carinii*. [The papers reviewed have been abstracted in this *Bulletin* ; see, for example, the summary of Recent Abstracts on Helminthiasis, this *Bulletin*,

1945, v. 42, 670.] The present authors tried to define :—(1) a dilution of the antigen at which false intradermal positive reactions due to intestinal nematodes can be eliminated ; (2) the sensitivity of subjects suffering from filariasis to the antigen. It was possible also to compare the results of the intradermal tests done on some subjects with those of biopsies done on the same subjects.

The antigen was made from *Dirofilaria immitis*, by a modification of the method of HUNTINGTON reported personally to the authors by MICHAEL. Dogs were killed by intravenous injection of magnesium sulphate and adult *Dirofilaria* were removed from their hearts. These were freed from blood clot and kept in running water overnight. They were then given several washes in distilled water followed by three changes of acetone. The nematodes were then dried in an incubator at 37°C. for 12 hours, by which time they were thoroughly dry. The authors found that if this temperature was exceeded, the antigen lost potency. The dried nematodes were ground up and the powder was kept in the refrigerator as stock from which fresh antigenic extract was prepared each month. The extract was made by making a 1 per cent. suspension of the powder in physiological saline, which was constantly stirred for 2 hours at 37°C., and then filtered through a Seitz filter ; phenol was added to a concentration of 3 per cent. This 1 : 100 extract was diluted to 1 : 200, 1 : 2,000, 1 : 4,000, 1 : 8,000 and 1 : 16,000. One contaminated batch of extract was re-filtered, and it was found that this process caused a loss of potency, a fact which was also reported by KING [*loc. cit.* above]. As a control, a fragment of the dog's heart was given the same treatment as the nematodes, and diluted 1 : 2,000. The tests were done by injecting 0·05 cc. of antigen intradermally into the volar surface of the forearm. One arm received the control and the 1 : 200 and 1 : 2,000 dilutions ; the other received the other dilutions. Results were read after 30 minutes, when positive reactions were at their height, and also after 24 hours. The authors took as a positive response a definite increase in size of the weal as compared with the control, together with erythema of 2 cm. diameter or more.

There were 65 subjects free from clinical filariasis, but infested with hookworm, *Strongyloides stercoralis*, *Ascaris lumbricoides*, *Enterobius vermicularis* and *Hymenolepis nana*. No positive reactions with dilutions above 1 : 2,000 were obtained in these subjects, with the exception of one who had herpes zoster as well as hookworm disease ; but this man was also positive to the control heart extract, and the authors, therefore, feel justified in ruling him out. They conclude that a dilution of 1 : 4,000 does not give cross reactions due to the presence of intestinal helminths. WRIGHT and MURDOCK [this *Bulletin*, 1944, v. 41, 1054] obtained cross reactions with *D. immitis* antigen at a dilution of 1 : 4,000, but they injected 0·1 cc. of the antigen, twice the amount used by the present authors.

The authors tested 91 subjects who showed clinical symptoms of filariasis. Of these 83 (91 per cent.) gave positive reactions to at least one of the dilutions used. In a controlled group of 18 subjects who had no history of having served in an area in which filariasis is endemic but who showed no clinical signs or symptoms of filariasis, 11 did not react to a 1 : 200 dilution of the antigen, 5 gave positive reactions to this dilution, and 2 to a dilution of 1 : 2,000. At the higher titres none was positive. The authors conclude from their results that a positive reaction at a dilution of 1 : 4,000 or higher indicates the presence of filariasis. Using this as a basis for interpretation of their results, they obtained a positive response in 78 per cent. of their subjects.

Comparison of biopsies of lymph nodes and skin tests done on the same persons showed that, in a group of 53 subjects, 74 per cent. were positive to dilutions of 1 : 4,000 and 1 : 16,000 of the antigen, and that biopsies in 60 per cent. of these were positive ; but in several subjects more than one biopsy was

needed to find a positive gland. In this group 10 showed negative biopsies but positive intradermal tests, and further biopsies might have been positive. In three subjects (6 per cent.) the biopsies were positive, but the skin tests were negative ; a similar finding was also recorded by DICKSON, HUNTINGTON and EICHHOLD [this *Bulletin*, 1944, v. 41, 303].

In 55 soldiers, all of whom had been exposed to filariasis, and some of whom had enlarged lymph nodes but were otherwise free from symptoms, positive intradermal reactions were obtained in 71 per cent. to dilutions of 1 : 4,000 and 1 : 16,000 of the antigen.

Complete blood counts were done on all those who had filariasis. There were no marked deviations in the number of erythrocytes, haemoglobin, neutrophils or lymphocytes, but 25 per cent. of the subjects showed an increase in the number of white blood cells, to 10,000 per cmm. or slightly more. The eosinophils were increased to 34 per cent. or more in the whole group of 91 men with clinical filariasis. When only those who gave positive skin tests to dilutions of 1 : 4,000 or higher were considered, it was found that 40 per cent. had eosinophilia, and 15 per cent. of these harboured intestinal helminths.

G. Lapage.

LEEDE, W. E. & JOSEY, A. I. **The Early Diagnosis of Filariasis and certain Suggestions relative to Cause of Symptoms.** *Ann. Intern. Med.* 1945, Nov., v. 23, No. 5, 816–22.

The authors studied 100 soldiers evacuated from various areas of the South West Pacific with filariasis. From only two of these men were microfilariae recovered. The diagnosis in the others rested on : (1) a history of residence in an endemic area ; (2) a history of symptoms suggestive of early filariasis ; (3) the clinical findings ; (4) the results of skin tests with filarial antigens ; and (5) the subsequent clinical course of the condition. There is great variation in the initial symptoms of infections acquired in different localities, but those from any one locality are constant. In general, however, after about one year's residence in an endemic zone an infected man experiences mild generalized aches and pains, testicular pains and malaise ; and a more or less generalized lymphadenopathy, and funiculitis, develop. Lymphangitis is of diagnostic importance, but is not always evident. In early cases, microfilariae will only very rarely be found in the peripheral blood.

The immediate evacuation of early cases from the endemic zone will result at least in the temporary subsidence and possibly in the complete disappearance of the disease—it is yet too early to state which with certainty. The available evidence indicates that avoidance of reinfection, or removal to a temperate climate, or both, result in diminution of the frequency and severity of the symptoms, and in recession of the physical signs of the infection.

The causation of the symptoms and signs of early filariasis is difficult to explain on the basis of mechanical obstruction by the parasites, such as leads to the irreversible changes seen in the later stages of the disease. An inflammatory or allergic tissue response appears a more probable explanation ; the sudden onset and evanescent nature of the initial symptoms and signs, with an associated eosinophilia, suggest an allergic basis for their occurrence.

A. R. D. Adams.

GOODMAN, A. A., WEINBERGER, E. M., LIPPINCOTT, S. W., MARBLE, A. & WRIGHT, W. H. **Studies of Filariasis in Soldiers evacuated from the South Pacific.** *Ann. Intern. Med.* 1945, Nov., v. 23, No. 5, 823–36. [18 refs.]

This is a report on the investigations made on soldiers repatriated to the United States from the small islands in the South Pacific as early cases of

Bancroftian filariasis. The clinical symptoms and signs of the disease were of minor severity, and accord with those described by other American workers.

The authors examined the intracutaneous test (both direct and passive transfer), and the complement fixation test in their series of cases. For these purposes they used antigens, prepared from *Dirofilaria immitis* and *Setaria equina*, diluted 1/4000 and 1/8000 ; the antigen controls were similarly diluted preparations of dog and horse protein. In addition, a series of non-filarial human controls was subjected to intradermal and complement fixation tests with the same antigens ; the results are set out in the text and in two tables. Some additional information is given of intracutaneous tests with antigens prepared from *Trichinella spiralis*, *Litomosoides carinii*, and *Ascaris lumbricoides* in varying dilutions, and also to Frei's antigen, in view of the importance of differentiating inguinal gland enlargements due to lymphogranuloma inguinale and to filariasis. The undesirability of using antigens in stronger solution than 1/8000 for intracutaneous tests is indicated, and there is a comment on the disappointing degree of specificity of both the intradermal and the complement fixation tests, and their correlation in diagnosis.

The authors conclude with the following summary :—

" 1. Clinical findings and results of intracutaneous and complement fixation tests in 145 soldiers evacuated from the South Pacific Area because of suspected bancroftian filariasis, are presented.

" 2. Signs and symptoms suggestive of filariasis including lymphadenopathy, lymphangitis, scrotal edema, funiculitis, orchitis and varicocele, arose on the average after about 13 months' residence in an endemic area.

" 3. The symptoms were, in general, mild and only six patients experienced bouts of acute lymphangitis during the period of study in the United States. No case of elephantiasis occurred. No case of chyluria was encountered.

" 4. Microfilariae were demonstrated in the blood on one occasion in each of four patients (in two of these at oversea hospitals).

" 5. In 47 patients eosinophilia of 4 per cent. or greater was found ; in eight patients the percentage was 10 or greater.

" 6. Microscopic examination of excised lymph nodes in 19 cases showed only a non-specific inflammatory response (' reactive lymph node '). No adult worms or remains of worms were seen.

" 7. In four of 29 cases roentgenograms of the scrotum showed tiny areas of calcification. However, it is not possible to state that such calcification was due to the presence of *W. bancrofti*.

" 8. Direct intracutaneous tests using antigens of *Dirofilaria immitis* and *Setaria equina* in 1 : 8,000 dilution gave positive responses in 54 per cent. of cases as compared with 6 per cent. in a series of 106 control subjects. Of 75 patients tested with 1 : 200 dilution of *Litomosoides carinii*, 77 per cent. gave positive reactions.

" 9. In passive transfer tests positive responses were obtained to either or both *D. immitis* or *S. equina* antigen in 1 : 8,000 dilution in 29 per cent. of cases. Of 50 patients tested with a 1 : 200 dilution of *L. carinii*, 46 per cent. gave positive reactions.

" 10. Positive complement fixation tests were found in 95, or 66 per cent., of 143 patients studied. However, the complement fixation technic used cannot be considered wholly specific since 16 to 25 per cent. of normal control subjects gave positive tests. It is believed that improvements being effected in the technic of the test will reduce the number of non-specific reactions. There was agreement between the results of the complement fixation tests and the direct intracutaneous tests with *S. equina* and *D. immitis* in 66 and 71 per cent. of patients, respectively.

" 11. No specific treatment was given. Therapy included a liberal diet, " reconditioning " by means of gradually increasing activity and psychotherapy to allay fears as to possible future complications of the disease. The outlook for the men is considered good because of the relatively short residence in the endemic area and the slight degree of infection." *A. R. D. Adams.*

WEBSTER, E. H. **Filariasis among White Immigrants in Samoa.** *U.S. Nav. Med. Bull.* 1946, Feb., v. 46, No. 2, 186–92, 1 graph.

These observations were made on 80 white men and women, civilian immigrants in Samoa who had lived there for at least 10 years. The examination consisted largely of questions regarding their histories and circumstances of life in Samoa, signs and symptoms of filariasis and the dates of their appearance; little importance was attached to the examination of blood films for microfilariae except in special cases, and physical examination was limited to cases of elephantiasis. Eleven had also lived in other endemic areas of filariasis but most had not been exposed to infection until they were nearly 30 years of age and had been exposed afterwards for over 25 years.

Symptoms and signs of filariasis were present in 27 of 54 men and 11 of 26 women; the incidence of filariasis was related to the degree or amount of exposure and therefore to occupation [the numbers are small]. Figures are given for the average time of appearance of the initial symptoms in males and females and the parts of the body affected. Many gave a history of several attacks of lymphangitis and fever in a year. There were 15 persons with elephantiasis; their ages ranged from 41 (very slight) to 78 (severe), average 64 years, and the average duration of exposure to infection was 35 years. The relation to the number of acute attacks is shown in the following table:—

Recurrence of acute symptoms.

Number of recurrences ...	1–10	11–20	21–40	41–60	over 60
Without elephantiasis ...	17	2	2	2	0
With elephantiasis	0	5	2	4	4

There was only one case of severe elephantiasis, in a trader aged 78, with both arms and both legs affected. *J. F. Corson.*

SCHLOSSER, R. J. **Observations on the Incidence of *Wuchereria bancrofti* Larvae in the Native Population of the Solomon Islands Area.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 493–5.

Thick blood films, taken at various times by day or night from some hundreds of natives of three of the Solomon Islands (Guadalcanal, Malaita and San Christoval), from natives of the Gilbert Islands and of the Fiji Islands, were examined for microfilariae of *Wuchereria bancrofti*; the parasites were found in about 20 per cent. Other observations showed that there was a definite periodicity, the night blood containing far more microfilariae than the day blood, the difference in numbers being more marked in natives of the Solomon Islands than in those of the Gilbert Islands.

Some feeding experiments were made in the Gilbert Islands with *Aëdes punctulatus punctulatus* and *Aëdes punctulatus farauti*; the microfilariae did not survive for more than 36 hours in the former species, and in one only out of 24 of the latter did microfilariae live for more than four days. The author states

that Byrd and St. Amant have demonstrated that in the Solomon Islands the microfilariae will readily develop to the infective stage in *Aëdes punctulatus farauti*. *J. F. Corson.*

Danglade, J. H. & Fitzgerald, P. J. **Asymptomatic Microfilariemia in the Caribbean Area.** *U.S. Nav. Med. Bull.* 1946, Feb., v. 46, No. 2, 193–201, 2 figs. [22 refs.]

Microfilariae of *Wuchereria bancrofti* were found in the night blood of 9 negroes of St. Croix, Virgin Islands, who gave no history of having had signs or symptoms of filariasis and in whom none could be found on physical examination. In blood taken between 11 and 12 o'clock at night no microfilariae were found in fresh preparations, they were seen in stained thin films in 5, and in stained thick films in 7 ; by the use of a modification of a concentration method (Knott) in which 2 cc. of blood were mixed with 10 cc. of 2 per cent. formalin and centrifuged at 2,000 r.p.m. for 5 minutes, and the stained sediment examined, the microfilariae were found in the remaining two patients. [See also O'Connor and Beatty, this *Bulletin*, 1938, v. 35, 761.] *J. F. Corson.*

Babione, R. N. *Mumu.* **A Few Facts about Filariasis for Folks who fear that Filaria-infected Fellows will fetch Filariae from the Front.** *Hawaii Med. J.* 1945, Nov.–Dec., v. 5, No. 2, 69–71.

The author's summary expresses completely the contents of the paper :—

" 1. Our cases suffer *mumu*, an allergic response to worm protein, but do not produce microfilariae *in the blood*, at least in demonstrable numbers.

" 2. It takes years of intensive exposure to develop a good micro-filaria-producer. Our men have not had that exposure.

" 3. In most of our men, the worms will probably all die before the man is desensitized ; if some should survive, they will not be in large numbers, nor have sufficient life-expectancy to produce secondary micro-filaria-carriers.

" 4. Transmission in the homeland will be inefficient also because of the average citizen's aversion to mosquitoes, and the extreme paucity of the reservoirs of micro-filariae.

" 5. Filaricidal drugs are known. They can be used if needed, to control transmission. At present they are still in the experimental stage, and they appear to aggravate the symptoms of *mumu*." *J. F. Corson.*

Sen, K. & Ghose, N. **Ocular Gnathostomiasis.** *Brit. J. Ophthalm.* 1945, Dec., v. 29, No. 12, 618–26, 1 text fig. & 1 pl.

A case of *Gnathostoma spinigerum* in the anterior chamber of the eye is described by Sen and Ghose. This is probably the first recorded case of this worm in a human eye. The onset occurred with a dull aching pain on the left side of the nose, extending to the left frontal and temporal regions. Swelling of the face then occurred, extending from the angle of the mouth to the roots of the hair, and was followed by orbital cellulitis, vitreous and retinal haemorrhages. Later the patient had two attacks of iritis with the development of grey nodules on the iris, which completely disappeared, leaving grey depressions. This was followed by two more attacks of iritis with the development of a single pigmented nodule on the iris in each attack. The pigmented nodule completely disappeared, leaving no mark after the first attack. In the second attack, which was the more severe, the pigmented nodule was seen to be the worm. The worm was removed at operation and the eye made an uneventful recovery, though optic atrophy developed. The habit of the *Gnathostoma* of burrowing through the tissues and migrating from place to place explained all

the signs, especially the inflammation, which, before subsiding in one place, appeared in a contiguous place in quick succession.

The size of the worm was as follows :—Length 3·5 mm., maximum width 0·41 mm., level of maximum width 0·41 mm. from the anterior end, width of the head 0·25 mm. ; the number of rows of spines on the head bulb was 4. The authors are of the opinion that if the infection took place through the gastro-intestinal tract, it must have been through swallowing infected *Cyclops* in drinking water. It was not clear how the worm came to the side of the nose from the stomach without causing any sign or symptom. The probable area of its entry into the eyeball from the orbit could be seen as a scar just below the macula. *E. O'G. Kirwan.*

Whittier, L., Einhorn, N. H. & Miller, J. F. **Trichuriasis in Children. A Clinical Survey of Fifty Cases and Reports of Three Cases with Heavy Infection and Striking Clinical Symptoms.** *Amer. J. Dis. Children.* 1945, Nov.–Dec., v. 70, No. 5, 289–92.

The authors have analysed the symptoms and treatment of 50 children infested with *Trichuris trichiura* and show that the symptoms may be serious and severe ; even fatal cases have been reported, though none of those under the authors' observation died. All 50 were admitted to the paediatric ward of the Gorgas Hospital, Ancon, during the years 1941–43. Three came from well-sanitated areas of the Canal Zone ; 22 from overcrowded districts with fair sanitation provided but not fully utilized, and 25 from semi-rural communities living amid primitive conditions. The ages of the patients ranged between 12 months and 12 years ; 28 were under 7 years old ; 28 were boys, 22 were girls. The common complaints were abdominal distress or pain in 9, diarrhoea in 7, blood in the stools in 5, vomiting in 5, fever in 3 ; but many of the patients were in hospital for other diseases than mere trichuriasis, so evaluation of these complaints is not possible. In only one was the pain suggestive of appendicitis, whereas Swartzwelder had recorded 16 out of 81 in whom the abdominal pain was localized in the right lower quadrant [see this *Bulletin*, 1940, v. 37, 660]. The authors found that the typical history was of diarrhoea of 1 to 3 months' duration, latterly stools streaked with blood, recurrent pain in the abdomen with tenesmus, loss of weight and rectal prolapse ; the worms were often seen by the parents in the wall of the prolapsed bowel. Twelve of the patients had eosinophilia from 5 to 14 per cent., haemoglobin 60–70 per cent., and red corpuscles 3½–4 million per cmm., " values which compared favourably with those observed in well children in Panama." In the three cases detailed, leucocytosis, to 13,500, was present in one only ; in the others the count was normal and in none of the three was there any eosinophilia ; in two no eosinophiles are mentioned, only polymorphonuclears and lymphocytes, and in the third the " differential count [was] within normal limits."

The best treatment, in the authors' view, is hexylresorcinol crystoids *per os*, combined with retention enemata of hexylresorcinol, 1 : 1,000, but in each of the three cases detailed it will be observed that, though general improvement took place, the patient on discharge from hospital still had ova of *Trichuris* in the stools. *H. Harold Scott.*

Neghme R., A. Epidemiologia de la Triquinosis. [**Epidemiology of Trichiniasis.**] *Biológica.* Santiago. 1944, Sept., No. 1, 127–40, 1 graph. [11 refs.] English summary.

" The author analyses some of the causes which determine the endemic state of Trichinosis in Chile, and indicates frequency attained in rats, hogs and in man.

" Trichinosis in rats has been stated in Santiago (5%) and in Concepción (7·8%) ; trichinosis of pigs, in the slaughterhouses all over the country, in quantities which range from 0·1% in the towns of the North (Antofagasta), up to 6% in some small towns of the South (Quirihue).

" In man, several Trichinosis epidemics have been discovered during the last 50 years, in different towns of Central and South Chile. The author has collected, from 1940 to 1943, 148 cases of Trichinosis, diagnosed mostly by means of Bachman's intradermic reaction. The inquiries on sub-clinical Trichinosis, carried out in 294 corpses of the Santiago hospitals, by Martinić as well as by the author, showed a 12·5% infestation with *Trichinella spiralis*. Investigations carried out with Bachman's intradermic reaction in healthy persons, showed delayed positive reactions in 5 out of 96 tested individuals (5·2%)."

GOULD, S. E. **An Effective Method for the Control of Trichinosis in the United States.** *J. Amer. Med. Ass.* 1945, Dec. 29, v. 129, No. 18, 1251–4, 3 figs. [Refs. in footnotes.]

This is a useful review of the incidence and control of trichiniasis in the United States in which the author decides that the best and most economical method of controlling this disease in man and hogs is the processing of pork products. No new facts are recorded in the review, but some of the facts given are in themselves interesting.

Recent surveys of the incidence of *Trichinella spiralis* in human post-mortem material in the United States have shown that the average incidence is 16 per cent. (see GOULD, S. E., " Trichinosis," 1945, Springfield, Ill., Charles C. Thomas). More thorough methods of examination have shown that the incidence in some areas may be as high as 36 per cent. (see EVANS, *J. Infect. Dis.*, 1938, v. 63, 337).

The incidence of *Trichinella spiralis* in hogs in the United States during the last 50 years has not varied from 1·5 per cent. It is possible that each American during life may eat nearly 200 meals of pork infested with Trichinella, and it is, therefore, not surprising that 16 per cent. of human diaphragms examined at autopsy contain larvae of *Trichinella*. The morbidity rate from trichiniasis is not definitely known, because many infestations are subclinical and, even when symptoms occur, they may not be correctly diagnosed ; but the mortality rate of cases clinically diagnosed is 5 to 6 per cent.

Discussing methods of control, the author says that little progress has been made during the last 50 years in the control of trichiniasis. About 70 per cent. of the pork products made in the United States are made in plants under Government supervision ; they carry the label " U.S. inspected and passed " ; but this label on non-processed pork products does not mean that these are free from viable *Trichinella* larvae. Meat packing plants which are under Government inspection must observe Federal regulations for processing pork of the kind usually eaten uncooked, and this pork " may be expected to be " free from viable larvae. But pork prepared in other plants under Federal inspection, and all pork not under Federal inspection, may contain living *Trichinella* larvae. Sausages are especially dangerous, because they are often eaten raw or insufficiently cooked. Because only about 70 per cent. of pork is produced under Federal inspection and because even in these plants it is only the processed pork which can be expected to be free from living *Trichinella* larvae, most of the American pork which goes to the kitchen may contain living larvae. Further, pork may be put in other foods (meat loaf, frankfurters, etc.) or bought in shops and, if this is eaten uncooked, it is dangerous. During

recent years there have been numerous lawsuits against packers because of illness or death, with remarkably high awards for the plaintiffs.

The incidence in American hogs of 1·5 per cent. is in sharp contrast to the incidence in hogs in Canada (0·57 per cent.), Poland (0·05 per cent.), Germany (0·001 per cent.) and Copenhagen (0·00075 per cent.).

The following methods of control are discussed by the author: (1) Destruction of rats. The author considers that pigs rarely eat rats and that, although it is wise to exterminate rats, they play only a small part in spreading trichiniasis.

(2) Education of the public. This is advisable, but is by itself of little value.

(3) Skin-testing of hogs. The author quotes the opinion of B. SCHWARTZ (*Ann. Rep. Smithsonian Inst.*, 1939, 413) that this is not a reliable method of determining the incidence in hogs. [But see the flocculation slide test of SUESSENGUTH and KLINE, this *Bulletin*, 1946, v. 43, 360, and the opinion of these authors that their method is a valuable means of determining the incidence in hogs.]

(4) Microscopic inspection of pork. This has proved "quite effective" in some countries and has been used extensively in Germany. The author concludes that systematic enforcement of it almost eradicated trichiniasis from Germany. Other countries which require microscopic inspection of pork are Denmark, Sweden, France, Argentina and Chile. The United States required it to be done from 1891 till 1906, but only for pork intended for export. Bismarck in 1880 and 1883 prohibited the import by Germany of American pork and even when, in 1891, microscopic inspection was instituted in the United States, Germany required its reinspection and in 1898 refused to accept the United States' certificate that the pork was free from *Trichinella*. [For another discussion of this aspect of meat inspection for Trichiniasis in America see also SCHWARTZ, *J. Amer. Vet. Med. Ass.*, 1941, v. 98, 458]. Microscopic inspection was abandoned by the United States in 1906. It has never been applied to pork eaten in the United States. It takes much time, although phototrichinoscopes have made it possible to throw on a screen images of several samples of meat from each hog. Further, this method may miss infestations when the larvae are young and are not encysted or are in uncalcified cysts, because then it is difficult to see them, and most hogs in the United States are slaughtered when they are less than a year old, *i.e.* when any larvae in them are in this condition. Also portions of pork may be examined which do not contain larvae although they are present elsewhere in the hog examined. Microscopic inspection may also give the public a false sense of security.

(5) Elimination of garbage and offal from hog feed and the cooking of garbage given to hogs. Cooked garbage is given to hogs in Canada, England, the Hawaiian Islands and the American States of Kentucky, Oregon and New York; it has been repeatedly advocated and would greatly decrease the incidence of *Trichinella* in hogs. Yet 0·9 per cent. of grain-fed hogs are trichinized (see SCHWARTZ, *J. Amer. Vet. Med. Ass.*, 1938, v. 92, 317). This method could not be enforced, except upon large breeders. In the American States named above the difficulties of enforcing it have made this method ineffective, and in Oregon State people can feed hogs on garbage from their own houses. A large corps of inspectors and others would be needed to enforce this method.

(6) Processing. This measure includes freezing, cooking, smoking, curing, etc. Larvae of *Trichinella* are killed by a temperature of 55°C.; but Federal regulations require that all parts of meat heated to kill these larvae shall be heated to 58·33°C. (137°F.). Freezing is chiefly used for processing pork. AUGUSTINE (*Amer. J. Hyg.*, 1933, v. 17, 697) showed that raw pork in commercial quantities can be freed from *Trichinella* larvae by a temperature of −35°C. (−31°F.); BLAIR and LANG, *J. Infect. Dis.*, 1934, v. 55, 95) found that freezing

at −17·8°C. (0°F.) for 72 hours killed these larvae. Most of the " deep-freeze " cabinets used in homes give temperatures varying from 0 to 5°F. and these can be maintained. This method would cost relatively little and would, by killing larvae in any scraps of pork which reach hogs, quickly reduce the incidence of trichiniasis in hogs and would check its spread in man. *G. Lapage.*

Pérez Ara, A. & Pérez Vigueras, I. Sur un nouveau nématode découvert dans la paupière de l'homme. [**On a New Nematode discovered in the Human Eyelid.**] *Bull. Soc. Path. Exot.* 1941, v. 34, Nos. 4/7, 104–7, 2 figs.

This note records the removal from the lower eyelid of a Cuban, aged 27, of fragments of two unidentified nematodes. About a week before he was seen, the patient noticed a very small swelling in his right lower eyelid, which caused him no inconvenience. This swelling appeared to be a non-inflammatory slight thickening about the size of a small pea in the external third of the lower eyelid, 1 mm. from its free border. It was elastic to the touch and not painful on pressure. The adjacent conjunctiva was normal. When it was removed, the swelling was yellowish-white with yellowish-white granular contents. From it emerged spontaneously two filiform, motile organisms tapering at both ends and resembling worms. These were fixed and examination showed that they were the caudal ends of two female nematode worms, both of which were gravid. The anterior ends were not found. One fragment was 7 mm. long, the other 3 mm. The maximum diameter of each was 220 microns. The cuticle was relatively thick, with transverse striations only at the caudal extremity, although longitudinal striation was evident throughout the length of the fragments and especially on the ventral and lateral surfaces. There were no cuticular spines, papillae or lateral alae. The anus was 260 microns from the caudal extremity and the vulva 837 microns from it. The vulval opening was transverse to the long axis of the body. The vagina was cylindrical and relatively large. The uterus contained shelled eggs, elliptical in form, smooth and easily seen ; they measured 20 to 23 microns long by 12·6 to 13·5 microns broad. Some were segmented and some contained embryos. There was no ovijector. No trace of the oesophagus was found in the larger fragment 7 mm. long, so that the authors concluded that a good part of the anterior end was lacking. The eggs were, the authors remark, considerably smaller than those of nematodes parasitic in man. They could not identify the nematodes.

G. Lapage.

DEFICIENCY DISEASES.

Sen, P. C., in collaboration with S. C. Seal. **Types of Oedema Cases seen in a Rural Area in Bengal.** *J. Indian Med. Ass.* 1945, Dec., v. 15, No. 3, 67–74 & 76, 1 sketch map & 1 graph.

Nine cases were studied in considerable detail. There is a general tendency to regard oedema, especially oedema of the extremities and occurring in Bengal, as " epidemic dropsy". The plan of investigation included :—(*a*) General Case Schedule, for information of identity, history, dietetic habits, etc. ; (*b*) Nutritional Assessment Card with information obtained from physical examination of the patient ; (*c*) Economic Survey Schedule, for information as to income, expenditure, economic status, etc. ; (*d*) Diet Survey Schedule, for recording the quantities of various foods taken during a period of 7 days.

Six families were involved. The information mentioned under each of the above is presented in a series of Tables and the upshot was that five of the nine

cases were diagnosed as epidemic dropsy (in two families which used mustard oil containing Argemone oil) ; three were associated with nutritional deficiencies, notably of vitamins A, B_1, B_2, and C ; the ninth was a case of oedema with anaemia secondary to chronic dysentery. The last four were infested also with ankylostomes, which may have played a part in causing the oedema.

H. Harold Scott.

Hughes, W. **Fatty Liver and Malignant Malnutrition.** [Correspondence.] *Lancet.* 1945, Dec. 29, 861–2.

In this letter Hughes draws attention to the part played by ariboflavinosis in the aetiology of malignant malnutrition with fatty liver. He shows that ariboflavinosis is the most outstanding feature in the epidemiological and clinical pattern of kwashiorkor—there is a high incidence of ariboflavinosis in the adult population of Southern Nigeria, the lesions of kwashiorkor are similar to those of ariboflavinosis, and both have parakeratosis as the underlying epithelial histological process, the mode of death in kwashiorkor may be sudden, with coma, as in dogs suffering from ariboflavinosis. Sebrell [*Bull. of Hygiene*, 1930, v. 5, 374] has shown that deprivation of riboflavin in dogs may lead to fatty liver and death in coma. Riboflavin, however, will not bring about recovery in the late stages, and Hughes suggests that deficiencies in other vitamins may be present.

Deficiency of riboflavin may be prevented by the use of milk or yeast in the diet. Milk is expensive, and in the tsetse belt of Africa may be impossible to obtain, but food yeast, at a cost of less than a farthing a day, would prevent the condition. *Charles Wilcocks.*

Reingold, I. M. & Webb, F. R. **Sudden Death following Intravenous Injection of Thiamine Hydrochloride.** *J. Amer. Med. Ass.* 1946, Feb. 23, v. 130, No. 8, 491–2. [13 refs.]

" 1. Sudden death followed an intravenous injection of a solution of thiamine hydrochloride.

" 2. The patient had been given four injections at frequent intervals prior to death. Following the last injection she complained of a generalized burning, perspired profusely, became dyspneic and cyanotic and soon died.

" 3. The death is considered an example of an anaphylactic shock, the thiamine hydrochloride being the anaphylactogen.

" 4. Pathologically, the anaphylaxis probably manifested itself in constriction of the smooth muscles of the pulmonary arteries and bronchioles, resulting in pulmonary engorgement and right heart dilatation and failure, and in mild pulmonary emphysema, respectively. In addition, small foci of polymorphonuclear leukocytes and round cells were seen in thickened septums of pulmonary alveoli. Foci of pigmented macrophages probably indicated that previous hemorrhages had occurred following an anaphylactizing injection."

HAEMATOLOGY.

Murphy, R. C., Jr. & Shapiro, S. **The Pathology of Sickle Cell Disease.** *Ann. Intern. Med.* 1945, Sept., v. 23, No. 3, 376–97, 6 figs. [42 refs.]

In sickle cell disease the sickling is an inherent property of the red cell and is determined by the ratio of oxyhaemoglobin to reduced haemoglobin within the cell. It appears that each cell has a specific threshold, or level of haemoglobin in the reduced form, at which it will sickle. Once this threshold is

reached sickling is abrupt and almost instantaneous, but the process may be reversed by crossing the threshold in the opposite direction by oxygenation. As normoblasts, reticulocytes, and cells showing polychromatophilia or other evidence of immaturity are very rarely seen in sickled form, it would seem that sickling is also a function of age of the cell, and that the sickling threshold decreases as the cell ages.

Presumably the threshold for sickling is first reached under conditions prevailing in the venous blood, so that the cell sickles only as it emerges from the venous end of the capillary, and resumes normal shape upon reoxygenation in the lungs. As the cell ages and its sickling threshold is progressively lowered, the sickling change will occur more and more towards the arterial end of the capillary, until finally the threshold passes below the oxygen tension of arterial blood. At this point the cell becomes permanently sickled.

A cell on becoming sickled loses the almost jelly-like flexibility of the normal cell and appears as fixed and rigid as a crystal of ice, while its length may be from two to five times the original diameter of the normal red cell. Consequently, capillary blockage, with stasis and subsequent thrombosis, readily occurs. With each thrombosis there are liberated into the circulation certain coagulant bodies, thrombin and thromboplastin, which further enhance the stasis and consequently the formation of sickle cells, and also lead to the formation of the thrombi found in the larger blood vessels. With the stasis a self-accelerating sickle cell " crisis " is inaugurated which gains momentum until most of the cells which will sickle are involved. The process tends to end when these cells have been removed from the circulating blood. This leaves a high proportion of young cells, and a quiescent period ensues. As these young cells mature they become increasingly more susceptible to the sickling tendency, with a resulting gradually increasing accumulation of sickled forms, until finally a new crisis is precipitated. Typical crises begin abruptly, which suggests that once this process starts the sickled cells precipitate out in a massive capillary blockade more or less simultaneously, and that the major part of the vascular thromboses associated with the crisis probably occurs within a few hours of its onset.

Dicumarol, with or without salicylates, and heparin, given to a patient after the onset of a crisis, failed to produce any amelioration of the symptoms. If anticoagulants are to be of any use at all they must be present immediately the crisis commences. Even if anticoagulants used at the beginning of a crisis were to postpone the thrombotic tendency of the blood, they could not, however, prevent the increased tendency of the cells to sickle as they grow older, which tendency leads inevitably to the vascular occlusions.

The supposition that the vascular occlusions occur very early in the crisis is not incompatible with its clinical course. The several days of fever, pain and other constitutional symptoms represent the period during which the multiple infarctions are resolving and the circulation is being restored. The haemolytic manifestations of the disease represent resolution of the thrombi, and also mechanical breakdown of the brittle sickled cells impacted in the capillaries. *F. Murgatroyd.*

SPIES, T. D. **Treatment of Macrocytic Anaemia with Folic Acid.** *Lancet.* 1946, Feb. 16, 225–8, 2 figs.

The synthesis of folic acid, a vitamin which is present in liver, yeast and other food materials, and which has a potent anti-anaemic action on certain forms of macrocytic anaemia, was announced in 1945 (ANGIER *et al.*, *Science*, 1945, Aug. 31, 227). The present paper enlarges the reports of its therapeutic action, which have already appeared [see this *Bulletin*, 1946, v. 43, 474].

When given either by mouth or parenterally, folic acid produced a prompt haematopoietic response in 26 patients suffering from macrocytic anaemias; these cases comprised five patients with nutritional macrocytic anaemia, five with Addisonian pernicious anaemia, eight with sprue, three classified as indeterminate, three with macrocytic anaemia of pregnancy, one with macrocytic anaemia associated with alcoholic addiction, cirrhosis of the liver, and neuritis, and one with macrocytic anaemia associated with carcinoma of the stomach. In the 26 patients "the initial red-cell count ranged from 1·1 to 2·97 million and averaged 1·87 million; on the fourteenth day it ranged from 1·58 to 3·57 million and averaged 2·69 million. The initial haemoglobin ranged from 5·9 to 9·9 g. and averaged 7·68 g.; on the fourteenth day it ranged from 7·1 to 11·7 g. and averaged 9·37 g. The first day of reticulocyte rise occurred from the third to the seventh day; the peak occurred on the third to the eighth day. The reticulocyte count at the peak ranged from 4·6% to 31·8% and averaged 17·2%." "Associated with the striking haematopoietic response was a remarkable subjective improvement in every case."

Determination of the minimal and average dose of folic acid requires further study, and there are indications that there is some variation in individual requirements. Doses ranging from 10 to 400 mgm. daily have been used for varying periods of time; when the dose was 20 mgm. or more, half of it was given in the morning and the other half in the afternoon. The larger dose (400 mgm.) has been given by mouth without ill-effects. Five patients have responded to the smaller dose (10 mgm.) administered by mouth; previously, one of these patients had failed to respond to 3 mgm., one to 4 mgm., and three to 5 mgm. administered by mouth daily for ten days. A total dosage of 20 mgm., parenterally or orally, is suggested tentatively.

No improvement was detected, either by clinical observations or by laboratory determinations, in three cases of aplastic anaemia, three cases of leukaemia, or in four cases of iron-deficiency anaemia, treated by folic acid. Only one patient with macrocytic anaemia failed to respond to 10 mgm. or more of folic acid; this patient, classified as a case of nutritional macrocytic anaemia although the type of the anaemia was never satisfactorily diagnosed, had a hypoplastic but not aplastic bone marrow and did not respond to liver extract given either by injections or by mouth over a period of four years.

F. Murgatroyd.

VENOMS AND ANTIVENENES.

SONNEBORN, D. G. **Poisonous Snake (Habu) Bites. Report of Eight Cases.** *U.S. Nav. Med. Bull.* 1946, Jan., v. 46, No. 1, 105–8, 2 figs.

Bites by *Trimeresurus mucrosquamatus* were far less common during the Okinawa campaign than had been expected. During three months, admissions to hospital for all causes numbered 6,500 [the number of men engaged is not stated], but there were only eight on account of snake-bite. This snake is reputed locally to be one of the most poisonous, but in the author's opinion systemic disturbance and toxic symptoms were unexpectedly mild, though local reaction was severe. Two men were bitten on the face, three on the wrist, and one each on the ankle, fingers and buttocks. One who received two bites on the face showed the most serious symptoms and is detailed here.

A private of the Marines, aged 20 years, was bitten on the cheek twice in rapid succession at 1 a.m. Swelling began immediately; in 5 minutes one eye was closed, and in an hour both eyes and the face were swollen and the swelling was extending down the neck. Nine hours after being bitten, he was admitted

to hospital. He complained of pain on swallowing, but there was no dyspnoea, no headache, vomiting or diarrhoea. Prior to admission he had been given ½ grain morphine sulphate, 500 cc. of whole blood and 1,000 cc. of saline intravenously (also, for some unexplained reason, 2 gm. sodii bicarb. *per os* every 4 hours). When he was admitted, the site of the bite was anaesthetic, and his speech was " thickened " from swelling of the lips, face and tongue. The face, scalp and neck were brawny with non-pitting swelling, there was no respiratory obstruction, no nervous symptoms were present and the reflexes were normal. Blood examination gave red cells 3,240,000 and white cells 8,000 per cmm. (87 per cent. polymorphonuclears). Ten cc. (one unit) of Brazilian antivenene was given intramuscularly, 9½ hours after reception of the injury. [Nothing is said of the constitution of this antivenene, but the statement is made that it was known not to be specific for the venom of this snake.] In another 8½ hours the oedema had involved the right shoulder and upper part of the chest in front, and there was some dyspnoea from swelling of the tissues. Fourteen hours later still, *i.e.* 32 hours after the bite, the swelling had spread all over the front of the chest, being more marked on the right side. The patient was coughing up some mucopurulent sputum. Penicillin was started [dose not stated] to guard against secondary infection. In two days there was no further swelling, nor any more dyspnoea, but the swelling had become ecchymotic. The pulse-rate had kept about normal, 70–80 per minute, and the blood pressure unaltered. On the fourth day the skin over the swollen area was purple to blue-black. Another blood count gave leucocytes 4,600 per cmm., with differential percentages normal. During the succeeding week the swelling gradually subsided, and a fortnight after his admission the patient returned to duty, the only residual symptom being slight swelling of the left cheek and upper eyelid.

Five of the eight patients received the Brazilian antivenene, at intervals ranging from one to ten hours after infliction of the bite and the author remarks : " such a small number of cases affords no true index of the value of the Brazilian antivenom ; however, it is the writer's opinion that those who received the antivenom late, or not at all, recovered as well as those who received it early." [In view of the specificity of most snake antivenenes, this is not surprising.] *H. Harold Scott.*

Wyon, P. H. **Four Cases of Russell's Viper Bite.** *Brit. Med. J.* 1945, Dec. 29, 919–20, 1 fig.

Four cases of snake-bite incurred in Central Burma are described, one of which was fatal. The snakes responsible were identified as Russell's vipers, apparently by the author. The identity of the largest, which measured 4 ft. 6 in., was confirmed by the local district laboratory.

The routine treatment is described in detail. A tight tourniquet was applied to the limb above the bite, and antivenene was at once given intravenously. The patient was anaesthetized with pentothal, and incisions were made " in the line of the bite " down to, but not through the deep fascia, unless the fascia had been penetrated by the bite. The cases were then " treated . . . by venesection from the affected limb and by retaining a venous tourniquet for as long as 18 hours. By releasing the tight tourniquet regularly, intermittent venesection was achieved." Later the patient was transfused if necessary.

The author discusses certain clinical aspects of snakebite and its treatment.

Most unfortunately, no autopsy was carried out in the fatal case. This patient was given antivenene soon after being bitten on the right wrist, and was

" first seen by the surgeon " about 8½ hours later. He died, as far as can be made out from the case history, about 29 hours after the bite.

B. G. Maegraith.

DERMATOLOGY AND FUNGUS DISEASES.

MOURÃO, B. M. O papel do estreptococo no pênfigo foliaceo (fogo selvagem). Estudo clinico-bacteriologico. [**The Part played by Streptococci in** *Pemphigus foliaceus* (**Wild Fire**). **Clinical and Bacteriological Study.**] *Mem. Inst. Butantan.* 1943, v. 17, 141–285, 28 figs. & 8 graphs. [83 refs.] English summary.

Though this monograph first saw the light nearly three years ago, it may be regarded as up to date since no work has been done on the subject in the interval. It may be looked upon as a complete monograph on *pemphigus foliaceus* and its association and possible aetiological connexion with streptococci. It comprises more than this, for it includes a brief review of the rôle of streptococci in dermatology.

The whole is divided into twelve chapters of which the first is introductory and the last two sum up the rest. The introductory chapter tells of the investigations of LINDENBURG on *pemphigus foliaceus* and Duhring's *dermatitis herpetiformis* and his conclusions that the former was an infective disease due to a virus which circulated in the blood and was transmissible to laboratory animals, notably rabbits and guineapigs. Others, however, and the present author among them, were unable to confirm this and took up the study afresh, this time from a bacteriological angle " to investigate methodically the pyogenic bacteria in pemphigus and dermatoses generally, bullous or otherwise." The second chapter reviews previous published work on streptococci in dermatoses of the pemphigus group, and concludes that the organisms are not important primarily, but are ready secondary invaders of the bullae. Chapter III states the plan proposed, which includes skin culture, blood culture, bacterial study of material taken ante- and post-mortem ; identification of the types isolated, their toxins and their pathogenicity for laboratory animals. Chapter IV speaks of the material for study obtained from 160 cases of this disease, including 87 of the generalized chronic form, 36 in the primary bullous stage, 15 of general dermatosis, the dystrophic form, 12 with localized dermatosis or *formes frustes*, 8 in the regressive stage and 2 healed cases, one with cutaneous sequelae and one without. In chapter V details of the results are given. Skin cultures were made from 55 patients, among them 21 in the generalized chronic stage and 16 in the invasion stage ; cultivations were tried from the bullae, from crusts and from fluid obtained by puncturing the bases of bullae. Of 53 cases (2 had recovered) 43 had streptococci in the lesions. Not in a single one of those in the primary bulla stage, with clear fluid, were streptococci found, but in all those with purulent contents or those crusted over without exception. In the latter there might also be *Staph. albus*, *Staph. aureus*, *Bact. coli* and diphtheroids. In the *formes frustes* streptococci were isolated " from 25%, the haemolytic form in 12·5% and inert streptococci in 12·5% " [but only 8 cases of this form were examined by skin culture, so these figures would imply that haemolytic streptococci were found in one case only and the same as regards non-haemolytic streptococci. To state this as 12·5 per cent. of cases tends to mislead.]

Of four cases of Duhring's *dermatitis herpetiformis* two gave a growth of haemolytic streptococci, one of them associated with *Staph. albus* ; a third gave *Staph. aureus* only. Chapter VI tells of the results of haemoculture. This was done in 150 cases and streptococci were grown from 19 (12·6 per cent.),

17 haemolytic, 2 non-haemolytic ; staphylococci from 5 (3·3 per cent.), the remaining 84 per cent. were negative. No growth was obtained from those in the primary, clear bullous stage ; 12 out of 82 in the generalized chronic stage were positive (14·6 per cent.) [not 8 per cent. as stated, this being calculated not on the 82, but on the total of 150], Chapter VII is concerned with material obtained at autopsy from the spleen, heart-blood, liver and other organs. Streptococci were isolated in pure culture from 4, with other organisms—*Staphylococcus*, *Bact. coli*, *Diplococcus pneumoniae*, *Proteus vulgaris* and others—from 19. From the heart-blood of 23, streptococci grew in pure culture from 8, and with other organisms from 9 more ; from 24 spleens streptococci alone in 9, and in association with other organisms in another 9. In 2 out of 11 blood cultures made within 3 hours before death or during the agonal period, haemolytic streptococci were isolated. Chapter VIII deals with the identification of the organisms isolated, their microscopical, cultural and biochemical characters, serological classification, their pathogenicity to rabbits, guineapigs, white rats and camondongos. The next chapter deals with streptococcal toxins of the strains isolated, erythrocytolytic, erythrogenic and fibrinolytic. Chapter X is largely taken up by quotations from the literature on the association of streptococci with other skin diseases and with post-mortem invasion of the body by streptococci. The last two chapters sum up generally what has been stated above, and the author's conclusions may be epitomized briefly thus :—

(1) The toxin of streptococcal infection plays a large part in *pemphigus foliaceus*.

2. A haemolytic streptococcus, group A, was constantly isolated from the skin lesions, less often from the blood ; also from the heart-blood and organs after death, but it is to be remembered that rapid dissemination of these streptococci takes place in the early hours after death.

3. Antifibrinolysin is present in the plasma of pemphigus patients.

4. The gravity of the skin infection is directly connected with the presence and virulence of haemolytic streptococci.

5. The clear fluid in the bullae of the early stage is free from bacteria.

6. When generalization occurs, the cutaneous resistance is broken down, streptococci gain entrance and pass on to the general circulation.

H. Harold Scott.

Leon y Blanco, F. & Sanchez Garcia, Elvira. Sinonimia y distribución geográfica de la pinta, mal del Pinto o carate. [**Synonyms and Geographical Distribution of Pinta.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Dec., v. 2, No. 4, 233–43. [76 refs.]

The authors give the local names of this disease in the different countries in which it is known to be endemic. We cannot here reproduce the whole list, but a few of the more important may be of interest : In Mexico ; *Tiña* (in Tabasco and Chiapas), *pinto* (Central and Southern States), *curicua* or *quiricua* (Jalisco and Michoacán), *guaguana* (Nayarit) ; in Colombia, *carate* or variants of this name such as *carathes*, and *timanejo* ; in Peru, *pinta*, *caracha*, *obería*, *mancha* ; in Santo Domingo, *gusarola* and *busarola*, and in Haiti *boussarole* ; in Ecuador and Bolivia, *enfermedad azul* ; in Guadeloupe *piquete* or *picuiti* ; in parts of Brazil, *purú-purú* or *kurú-kurú*. Many others are given and also several based on the pathology, as *pannus carateus*, *syphyspyloria thelodérmica*, and the like.

The authors pass on to give an account of the geographical distribution of the disease, dividing the countries into three categories : (1) Those where it is known for certain to exist : Cuba, Mexico, Colombia, Venezuela, Ecuador, Peru, Brazil, Bolivia, Guatemala, Honduras and British Honduras. (2) Those where cases are recorded but it is not certain that they are actually mal del pinto :

San Salvador, Haiti, Santo Domingo, Porto Rico, the Virgin Isles, Panama, Argentina, the United States of America, Ceylon, the Philippines, the Gold Coast, Italian East Africa. (3.) Those where pinta-like conditions are found, but definitely not true pinta : Turkestan, where there is a condition known as endemic vitiligo, Turk's island, where there is a pinta-like condition known as Safú. [A useful list to have for reference.] *H. Harold Scott.*

Oteiza, A. & Leon Blanco, F. Un caso con manifestaciones cutáneas temprana de pinta. [**A Case of Pinta with Early Cutaneous Manifestations.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Dec., v. 2, No. 4, 199–205, 4 figs.

Pinta in a negress of 36 years is described ; she suffered also from rectal stenosis due to lymphogranuloma inguinale. The first sign of her present pinta state was a dark-coloured pruriginous patch on the flexor aspect of the right wrist ; this had gradually extended. For 3–4 months it was the only manifestation ; then others began to appear : one on the internal aspect of the right thigh, another on the external aspect, a third on the inside of the left thigh. After a further interval another appeared above the left knee, then the right and at the back of the right leg below the popliteal space. Spirochaetes were seen in material from all the lesions and the pintoid nature was proved by the fact that inoculation of the tissue fluid produced typical initial pinta lesions in volunteers. The patient had been shown at an earlier stage to the Cuban Society of Dermatologists. *H. Harold Scott.*

Iams, A. M., Tenen, M. M. & Flanagan, H. F. **Histoplasmosis in Children. Review of the Literature, with Report of a Case.** *Amer. J. Dis. Children.* 1945, Oct., v. 70, No. 4, 229–40, 5 figs. [Refs. in footnotes.]

The authors give summarized descriptions, collected from the literature, of the clinical and pathological features of 21 cases of histoplasmosis in children under 13 years of age : 15 were only 15 months old or less ; 12 were 8 months old or less, and the youngest patient was only 7 weeks old [see Schlumberger and Service, this *Bulletin*, 1944, v. 41, 606]. The apparent duration of the disease was from 1 week to 7 months ; the average being about 3 months. The symptomatology in infants differs from that in adults but, alone, it is not a sufficient basis for diagnosis. Skin lesions were present in four cases, and consisted of crusted, vesicular, pustular, scaly and gangrenous lesions associated with a generalized systemic infection. Pulmonary lesions, sometimes consisting of caseous nodules, were found at autopsy in 15 cases, and two of these infants had suffered from cough simulating pertussis. Gastro-intestinal symptoms, including loss of appetite, cyanosis when feeding, diarrhoea or constipation, and vomiting, were present in 9 infants, and in 13 cases intestinal lesions were present, consisting of ulceration of the mucosa with slight involvement of the lymph follicles. Splenomegaly and hepatomegaly were commonly present, with invasion of the sinusoids and parenchyma of the organs by macrophage cells loaded with *Histoplasma* ; but actual granulomatous lesions were uncommon. Generalized lymphadenopathy with moderate, painless and discrete enlargement of the lymph nodes was commonly encountered ; sometimes the glands showed caseous changes simulating tuberculosis. Microscopically, the normal structure of the lymph node was found to be replaced by myriads of macrophages laden with *Histoplasma*.

The diagnostic procedures recommended include biopsy of lymph nodes, spleen, bone marrow or cutaneous lesions. Blood smears occasionally show

the parasite, and blood culture may prove of value in diagnosis, but it necessitates some delay. The cutaneous sensitivity test with "histoplasmin" is, as yet, of undetermined diagnostic value. The prognosis is almost uniformly unfavourable. *J. T. Duncan.*

Niño, F. L. Granuloma paracoccidioidico. Estudio de una nueva observación en la República Argentina. (Nota previa.) [**Paracoccidioidal granuloma. Study of a New Case in the Argentine Republic. Preliminary Note.**] *Rev. Asoc. Med. Argentina.* 1945, July 30, v. 59, No. 562, 830–34, 7 figs.

This is a report of a new case of paracoccidioidal granuloma in which the infection appears to have been contracted in Buenos Aires. The patient, a man aged 44, was a trader in charcoal and maize, materials from which, the author considers, the infecting fungus may have been derived. The lesions were situated in the mouth and there was an associated mass of enlarged and suppurating glands, the size of a pigeon's egg, in the neck. The lungs were also involved and the parasite was found in the sputum and in material aspirated from the bronchi with the aid of the bronchoscope. The diagnosis was made by microscopical examination of the sputum, tissue obtained by biopsy, and pus from lymphatic glands, and was confirmed by cultivation of the fungus and by the results of the inoculation of morbid material into guineapigs.
J. T. Duncan.

TROPICAL OPHTHALMOLOGY.

i. Dansey-Browning, G. C. & Rich, W. M. **Ocular Signs in the Prisoner of War returned from the Far East.** *Brit. Med. J.* 1946, Jan. 5, 20–21. [11 refs.]

ii. Ridley, H. **Ocular Manifestations of Malnutrition in released Prisoners of War from Thailand.** *Brit. J. Ophthalmology.* 1945, Dec., v. 29, No. 12, 613–18.

iii. Garland, H. G. **Ocular Signs in the Prisoner of War from the Far East.** [Correspondence.] *Brit. Med. J.* 1946, Jan. 26, 143.

iv. Churchill, M. H. **Dietary Deficiency Diseases among Prisoners of War.** *J. Roy. Army Med. Corps.* 1945, Dec., v. 85, No. 6, 294–8.

i. The ocular signs of malnutrition in prisoners-of-war returned from the Far East are discussed by Dansey-Browning and Rich. They examined some 30 men who were released at the recapture of Rangoon, and who had been prisoners for 2 to 3 years. Ten subjects were found to have bilateral scotomata, with a "tail" to the white scotoma leading from the fixation spot towards an enlarged blind spot. There did not appear to be any "nuclei" lying between the blind and fixation spots. There was no constancy in the colour scotomata. In not one of these 10 subjects was there contraction of the peripheral visual field either to white or to colours. All 10 showed some degree of visual failure, and in five the corrected vision could not be brought above 6/60. The ophthalmological examination revealed that all 20 optic disks showed some degree of pallor. Four of the disks showed an apparent primary optic atrophy; four showed pallor of the papillomacular bundle, and eight showed pallor of the temporal half. No case showed ocular muscle paresis. No diminution of sensitivity of the cornea and conjunctiva was found, neither was there any evidence of xerosis, nor any of the ocular signs of ariboflavinosis.

The authors consider that there is a relationship between the scotomata to white and those of the toxic amblyopias, and that the deficiencies of vitamins B_1, B_2 and (very dubiously) A, appear to play their part in the ocular signs of beriberi, although the exact nature of the deficiency remains obscure. They conclude that, as the optic nerve is part and parcel of the c.n.s., the damage done to the nerve proper by the axial optic neuritis of beriberi is final, and that any improvement of vision can be but slight.

ii. The ocular manifestations of malnutrition in some 500 released Allied prisoners-of-war and internees from Thailand who considered that their sight had deteriorated during captivity are discussed by RIDLEY. Among these no fewer than 100 cases of amblyopia were seen in 17 days, and many of those whose corrected vision was normal had subclinical vascular lesions of the eyes. Visual failure occurred in 90 of these patients between October, 1942 and December, 1943, so that their sight had been defective for 2½ to 3 years. Acuity with correction varied between 1/60, and a partial 6/6, nine read less than 6/60 with the better eye, sixteen, 6/60, twenty-six, 6/36, fifteen, 6/24, fifteen, 6/18, seven, 6/12, eight, 6/9, and four, 6/6. All those with scotomata and good acuity reported recovery from temporary severe amblyopia. In many cases the onset had been sudden, maximum disability being reached within a single day, though in others it was gradual, taking months to develop. There was some degree of photophobia, and sight was particularly defective in bright light, but few of the subjects complained of difficulty in seeing at night. Many patients with amblyopia gave histories indicating that, in addition to recurrent attacks of the common tropical infections, they had suffered from pellagra, oedema of the lower extremities, dry beriberi, and from sore tongue and *perlèche*, which usually accompany deficiency in the B group of vitamins. A high proportion of the cases had become nerve deaf. In the fundus there may be no visible abnormalities even when the amblyopia is severe and of long standing, though in many of the severe cases there is definite pathological pallor of the temporal half of the optic disk, the colour becoming grey rather than pure white. There were 48 cases of optic atrophy, and 30 more were regarded as doubtful in this respect. Nothing was ever found that was suggestive of past oedema of the nerve head ; the retinal vessels were not constricted and the macular area and its surrounding vessels generally appeared normal, though in a few instances in which temporal pallor was marked there appeared to be some reduction in the calibre of the macular arterioles, a change probably secondary to retinal atrophy.

Campimetry revealed in 90 cases a small, sharply-demarcated central scotoma rarely extending more than 3° and sometimes only 1° from fixation, and often less, though within this area in severe cases even a 40-mm. white object was invisible at 1 metre. The edges of this scotoma are abrupt, its density rather than its size being the important variable. In the remaining 10 cases the core of the scotoma was para- or peri-central and situated within the 3° circle, the fixation area showing less visual depression. In this type the affected area was usually more extensive and the peripheral margin, especially, was less abrupt and extended as far as the 5° circle. In four of these cases the scotoma appeared to be limited by the horizontal meridian on both sides of the fixation point. Some patients with this type of field say that some portion of a letter or some letters in a line are invisible, and that objects tend to appear and disappear. In the majority of these cases there was a history of considerable improvement during captivity, which is in accordance with the shelving edge of the scotoma.

No defects were discovered in the peripheral fields.

Practically all the released prisoners showed some degree of keratoconjunctival abnormality. There was no gross injection, except occasionally in the interpalpebral area, where the conjunctiva might be dull, thickened or opaque. No

xerosis nor Bitot's spots were seen. In 96 per cent. of the amblyopic and 91 per cent. of the other patients the fine capillary plexus at the limbus was increased in extent, and minute superficial vessels extended as far as 2 mm. into the cornea. The vascularization was accompanied by superficial opacification. Frequently the internal margins of capillary loops united to form quite large circumferential vessels. The most striking feature of the limbal capillaries was their variability in size, which was often so great that aneurysms, both fusiform and saccular, appeared. These were situated rather more frequently on the scleral than on the corneal portion. Aneurysms were present in 65 per cent. of the scotomatous patients and in 48 per cent. of those with normal sight. No haemorrhages were observed. There seems little doubt that the lesions described are due primarily to malnutrition, though there may be other factors, since only a small proportion of men living under identical conditions were affected. There is no doubt that the diet was deficient generally, especially in protein and fats as well as vitamins; and, in the absence of direct evidence that avitaminosis unsupported by other factors is the cause, it seems advisable to attribute the lesions to general malnutrition rather than simple deficiency of the B group. The abnormal vascularity of the limbus suggests a deficiency of vitamin B_2, although healthy soldiers who have been in a tropical climate for some time have some increase in the limbal plexus.

It is uncertain whether the disturbance in the visual pathway originates in the retina or the optic nerve; nor is the mechanism whereby the neurones are affected understood. In view of the known abnormality of the conjunctival capillaries, it is tempting to postulate a vascular origin—failure of the choriocapillaris to nourish the outer layers at the macula or, if the limitation of some fields by the horizontal meridian has any significance, failure of the macular branches of the superior or inferior divisions of the central artery to nourish the inner layers of the retina. There is, however, no concrete evidence to support such a theory.

iii. GARLAND, in discussing the ocular signs in the prisoner-of-war from the Far East, considers these to be a constant feature in an interesting syndrome; there is also commonly bilateral nerve deafness, of a varying degree, with a spinal cord syndrome. The latter is usually a picture of posterior column dysfunction (but occasionally with pyramidal signs), the legs being affected more than the arms. In some cases the syndrome has been further complicated by intellectual deterioration. That this syndrome is due to a dietary deficiency seems almost certain, but it seems equally certain that it has nothing whatever to do with vitamin B_1. It is very doubtful whether it has anything to do with vitamin B_2, and certainly, in some of the cases, the syndrome has existed throughout its course with no evidence of beriberi or pellagra. At the same time, scrutiny of the diet on which the picture develops suggests that the deficiency is probably in the B group of vitamins, though a deficiency of vitamin A has not yet been excluded. Garland has little doubt that some of these subjects did, in fact, suffer from beriberi, but he suggests that the beriberi was a co-existing deficiency picture; he considers that the lesion underlying the visual failure lies in the optic nerve, but he does not describe it by the term "retrobulbar neuritis," as there is no proof that it is an inflammatory condition.

iv. Ophthalmic abnormalities occurring among nearly 500 cases of deficiency disease in prisoners-of-war in Singapore and Thailand during 1942 to 1945 are discussed by CHURCHILL. Avitaminosis amblyopia (neuroretinitis) was a common condition, the first cases appearing within four months of the prisoners going on to the Japanese ration scale. In August, 1945, in one camp in Thailand, 81 men out of 1,200 were affected; but a considerable number of men suffering from this condition had already died from other diseases. Of these 81 cases, 10 followed shortly on an attack of dysentery; in 16 there was an association with

beriberi; in 4 with stomatitis; in 3 with "happy feet" (nicotinic acid deficiency), and in 2 with pellagra. The outstanding symptom was a blurring vision, but this was preceded by a smarting of the eyes, lachrymation and photophobia. When working in the sunlight many of the patients experienced actual pain behind the eyes. The blurring was first noticed on reading, but soon some of the men were unable to recognize people or objects out-of-doors. The failure of sight was often progressive and severe; in other cases it progressed to a certain extent and then remained stationary; in others, again, it improved when there was any substantial improvement in the diet. These men had subjective scotomata, but rough tests revealed no impairment of the visual fields. Ophthalmological examination showed a retina which was often redder than normal, with swollen veins. The disk was pink, and its margins were frequently blurred; occasionally the temporal half of the disk was quite white. Among 72 cases, some degree of cupping or excavation of the disk was present in 36, and the lamina cribrosa was seen in 8. A puzzling feature of this disease was the apparent lack of correlation between the visual defect and the extent of the ophthalmoscopic changes.

Night-blindness was a rare condition among the prisoners-of-war, occurring in only 3 out of 1,200 men. It was associated with only 1 of the 81 cases of avitaminosis amblyopia. This comparative rarity was probably due to the fact that pumpkins, rich in carotene, were a fairly constant item in the ration scale. Four out of some 1,200 men suffered from corneal ulceration, and this was not more common among the prisoners than amongst British troops in the tropics.

E. O'G. Kirwan.

HEAT STROKE AND ALLIED CONDITIONS.

i. Spector, H., Mitchell, H. H. & Hamilton, T. S. **The Effect of Environmental Temperature and Potassium Iodide Supplementation on the Excretion of Iodine by Normal Human Subjects.** *J. Biol. Chem.* 1945, Nov., v. 161, No. 1, 137–43.

ii. ——, Hamilton, T. S. & Mitchell, H. H. **The Effect of Pantothenic Acid Dosage and Environmental Temperature and Humidity upon the Dermal and Renal Excretion of Pantothenic Acid.** *Ibid.* 145–52. [15 refs.]

iii. Shields, J. B., Johnson, B. C., Hamilton, T. S. & Mitchell, H. H. **The Excretion of Ascorbic Acid and Dehydroascorbic Acid in Sweat and Urine under different Environmental Conditions.** *Ibid.* 351–6.

iv. Johnson, B. C., Mitchell, H. H. & Hamilton, T. S. **The Occurrence of Inositol and of *p*-Aminobenzoic Acid in Sweat.** *Ibid.* 357–60.

These papers are based on results obtained during a "2-year study of the effects of high environmental temperature and variable humidity upon the dermal losses of certain minerals and vitamins and their metabolites." Five men aged from 20 to 28 years spent eight hours a day in an air-conditioned room five days a week. The conditions were alternate weeks "comfortable" (86°F. 50 per cent. relative humidity) and hot-moist (100°F. 69 per cent. relative humidity). Other conditions were sometimes imposed. The subjects were apparently at rest. Sweat losses calculated in the usual way were, for comfortable conditions, 80 gm. per hour, and for hot-moist conditions, 670 gm. per hour (averages from pooled results of the four papers; there is one inconsistency in that in the second paper subject C is shown as sweating

at 79 gm. per hour in week 28, and in the fourth paper at 27 gm. per hour ; this is not a misprint, as the averages for the group are correspondingly different]. The loss during comfortable conditions, though high, was attributed by the author to insensible perspiration [true insensible perspiration rarely exceeds 40 gm. per hour]. The mean sweat loss in hot-moist conditions varied between 581 gm. per hour and 814 gm. per hour for different weeks ; there was no regular variation attributable to acclimatization. " Sweat " (*i.e.* pooled skin excretions) was collected on waterproof sheets and on swabs, and was added to distilled water washings from the body, clothes and utensils to form for each subject, each day, a single bulk specimen for analysis containing all the skin excretions for that day. On Saturday mornings undiluted sweat was collected under hot-moist conditions by collecting the drips off the subjects as they stood in pans [no allowance was made for evaporation, though some probably occurred]. Faeces and urine were also collected and analysed.

i. *Iodine excretion.*—The loss of iodine in the insensible perspiration was 2·5γ per 100 cc. when no iodine supplement was being taken, but in frank sweat (" undiluted " samples) it was only 0·95γ per 100 cc. The total skin loss was, however, greater when sweating, 5·1γ per hour compared with 2·2γ per hour. A supplement of 2 mgm. potassium iodide per day did not affect the iodine losses in the insensible perspiration, but increased the losses in sweat from 0·95 to 3·65γ per 100 cc. (undiluted sweat) and from 1·5 to 17·7γ per hour. The urinary loss was in all cases more than 75 per cent. of the total excretion, but it was slightly less in hot-moist conditions, than in comfortable conditions when an iodine supplement was given, thus balancing the increased skin loss. Faecal excretion after extra iodine was greater in hot-moist than in comfortable conditions, but it was the same under both conditions without the supplement.

ii. *Pantothenic acid excretion.*—About 8γ of pantothenic acid were lost per 100 gm. insensible perspiration. Undiluted sweat contained 3·8γ per 100 cc. ; increasing the relative humidity did not significantly increase the concentration. Losses of pantothenic acid per hour from the skin were about 6γ under comfortable and 25γ under hot-moist conditions. Supplements of up to 16 mgm. calcium pantothenate per day did not increase the concentration in either insensible or sensible perspiration. Urinary excretion of pantothenic acid was slightly greater under hot-moist conditions, but the proportion of the total excretion found in the urine fell from 97·6 per cent. to 87·3 per cent. owing to the very much greater rate of excretion via the skin. Thirty-one per cent. of an 18 mgm. dose of calcium pantothenate was recovered from the urine. The authors discuss their results in relation to previously reported results by other workers, and attribute differences to the fact that they used *Lactobacillus arabinosus* as test organism, whereas others had used *Lactobacillus casei*, which may be stimulated by fatty materials in the sweat.

iii. *Ascorbic acid excretion.*—No rubber equipment was used in the study, as it has repeatedly been shown that sweat which has been in contact with rubber reduces 2, 6-dichlorophenol-indophenol and hence has an apparent ascorbic acid content, whereas sweat collected in other ways has no such reaction. By the indophenol method, only 9 out of 82 samples of sweat were found to contain ascorbic acid ; but by the 2, 6-dinitrophenyl-hydrazine procedure of Roe and Kuether, free ascorbic acid was found in five out of eight specimens tested, in a mean concentration of 33γ per 100 cc. By the same method an average of 70γ of dehydroascorbic acid was found per 100 cc. of sweat. In one experiment daily doses of 500 mgm. of ascorbic acid decreased the ascorbic acid content of the sweat from 33γ per 100 cc. in the control week to 5γ, while the dehydroascorbic acid content increased from 34γ to 107γ per 100 cc. In another period and with the same daily doses the dehydroascorbic acid content was only 66·5γ per 100 cc. The combined skin losses of ascorbic

and dehydroascorbic acids were equivalent to 2·74 mgm. only per day, even with profuse sweating, hence skin losses do not noticeably affect vitamin C requirements. Urinary losses of ascorbic acid were greater at high humidities than under comfortable or hot-dry conditions.

iv. *Inositol and p aminobenzoic acid excretion.*—The concentration of inositol in sweat was found to be 21γ per 100 cc. ; under hot-moist conditions the loss per hour was 0·118 mgm. compared with a loss of 0·027 mgm. under comfortable conditions. Urinary excretion was variable. The average concentration of *p* aminobenzoic acid in sweat was 0·24γ per 100 cc. *W. S. S. Ladell.*

BURCH, G. E. **The Influence of Environmental Temperature and Relative Humidity on the Rate of Water Loss through the Skin in Congestive Heart Failure in a Subtropical Climate.** *Amer. J. Med. Sci.* 1946, Feb., v. 211, No. 2, 181–8, 4 figs. [11 refs.]

Water losses were measured from three small areas of skin, first in a comfortable atmosphere (dry bulb 70°F., wet bulb 62°F., relative humidity 60 per cent.), and then in a hot humid atmosphere (dry bulb 104°F., wet bulb 93°F., relative humidity 64 per cent.). The areas chosen were : the tip of the index finger, on the shin, and on the volar surface of the forearm, all on the right side ; the measurements were made by directing a stream of dry oxygen over the skin and then condensing the water taken up, the amount recovered being estimated gravimetrically. Five groups of subjects were tested : (*a*) eleven normal subjects ; (*b*) ten patients with diseases other than congestive heart failure ; (*c*) five patients with slight to moderate failure ; (*d*) five patients with moderate to severe failure ; (*e*) ten patients with severe failure. Under comfortable conditions the losses were the same in all groups, with finger losses about 50 per cent. greater than skin and forearm losses. In hot humid conditions finger losses showed a 4-fold increase, and the other losses more than an 8-fold increase (compared with the losses under comfortable conditions) in the normal, non-heart failure and slight heart failure groups ; but in the moderate and severe heart failure groups finger losses increased only 2·5 times for both groups, and the other losses 4 times and 2·5 times, respectively. Thus local sweating in these two groups was impaired relative to the rest.

This impairment of local sweating is, Burch considers, a manifestation of congestive heart failure ; [he is no doubt correct, but he weakens his case by drawing his main conclusions from the comparison between a control group, average age 26, comprising nine white men, one white woman and one coloured woman, and a severe heart failure group, average age 54, comprising four coloured women, three coloured men, and one white man]. Diminished local sweating indicates, Burch argues, a generalized and " marked impairment of the emergency sweating mechanism .... predisposing .... to the accumulation of body heat." [He would be on surer ground if he had taken measurements from more areas, see WEINER, this *Bulletin*, 1946, v. 43, 249 ; no measurements are given of the body temperatures in any of the subjects, though reference is made to observations by other authors on pyrexia in patients with congestive heart failure in comfortable environments.] The ability to sweat, Burch states, returns with recovery of the cardiac function, but no serial observations on a patient during recovery are given in support of this. In his discussion the author emphasizes the importance of cool comfortable conditions for patients with congestive heart failure, in order to keep the demand on the cardiovascular system as low as possible ; and he therefore recommends air-conditioned wards, especially in warmer climates.

W. S. S. Ladell.

Koch, W. **Three Rapid Tests for the Estimation of Tropical Fitness of Fabrics.** *J. Hygiene.* 1946, Jan., v. 44, No. 4, 286–8, 3 figs.

The author suggests that the fabric for use in the tropics may be decided by considerations of its thermal insulation quality and its air porosity only. After describing how an estimate of insulating power can be obtained by comparing the cooling rate of a kata-thermometer " clothed " with the fabric, with the cooling rate when it is uncovered, this author discards this in favour of a simple measurement of thickness. Rees (*J. Textile Inst.* 1941, v. 32, T. 149) showed that thermal insulation, measured in the laboratory, is, among other things, a function of the thickness of the fabric ; Koch accepts this as applicable to physiological conditions, and describes a simple optical method of measuring thickness. Instead of measuring air porosity, he suggests that the head of pressure necessary to force mercury through an unsupported unstretched layer of the fabric should be determined. He found a correlation of −0·78 between this " mercury figure " and the air permeability ; the figures he gives relating the two values, when plotted fall accurately on a rectangular hyperbola and are probably therefore not his original experimental data. [Physical considerations would in any case suggest the hyperbolic relationship.]

[The author completely ignores other physical properties of fabrics, such as water vapour permeability and water absorbing power.] *W. S. S. Ladell.*

Baxter, S. **Heat and Water Vapour Transfer through Fabrics.** *J. Textile Inst.* 1946, Mar., v. 37, No. 3, T39–57, 15 figs. [11 refs.]

MISCELLANEOUS DISEASES.

Chalgren, W. S. & Baker, A. B. **Tropical Diseases : Involvement of the Nervous System.** *Arch. Pathology.* 1946, Jan., v. 41, No. 1, 66–117. [305 refs.]

Brinton, D. **An Unusual Form of Epidemic Food-Poisoning with Neurological Symptoms.** *Proc. Roy. Soc. Med.* 1946, Feb., v. 39, No. 4, 173–5 (Sect. of Neurology 5–7).

During 13 months, October 1942—November 1943, some 450 persons in Aden had suffered from *miscara* poisoning, from eating imported wheat contaminated by the weed flax-darnel, or *Lolium temulentum.* The local word *miscara* is said by the author to mean " tipsy " and the symptoms are very characteristic of this state : dizziness, headache, tremors, lassitude, slurred speech and staggering gait ; sometimes gastro-intestinal disturbance. If much has been taken the patient may become comatose for several hours. No deaths were reported. The condition recorded and the risks from eating contaminated Abyssinian wheat are well known and the fact that in ordinary circumstances cases of poisoning are rare is due to the care with which the weed is separated from the wheat.

The actual toxic element is said to be some pyridine base in the mould seen on nearly every weed-seed. [This form of poisoning has been known in India for many years. Concerning it the reviewer wrote in 1920 ; " *Lolium temulentum*, ' bearded darnel,' known as mostaki (Punjab) and moschni (N. W. Provinces). Bread made with flour partly constituted by the seeds of this plant sets up the following symptoms : vertigo, staggering gait, nausea, vomiting, dim vision (perhaps green), tremors of arms, legs and tongue, with dysarthria ; a burning pain in the mouth and throat, and general prostration with a weak, irregular

pulse. No fatal cases have been reported. It is not known whether the poisoning may not be due to an associated symbiotic fungus." *The Practice of Medicine in the Tropics.* Byam & Archibald, 1921, v. 1, 782.] *H. Harold Scott.*

Cohen, S. C., Emert, J. T. & Goss, C. C. **Poisoning by Barracuda-like Fish in the Marianas.** *U.S. Nav. Med. Bull.* 1946, Feb., v. 46, No. 2, 311–17, 2 figs.

Two outbreaks of food-poisoning are recorded in the same district, one affecting 41 persons of an officers' mess in a Military Government camp on Saipan; the other affecting 10 civilians (Koreans) in an internee camp on Saipan. The poisoning is ascribed to eating "barracuda-like fish," from which it would be inferred that the actual diagnosis was not made, but the article is illustrated by drawings of *Sphyraena barracuda* and *Ruvettus pretiosus* (oil-fish).

The fish eaten in the officers' mess was a large one, 55 lb., and was eaten 27 hours after being caught; at the internee camp the 10 poisoned were among 30 who partook of it, 8 hours after it had been caught. Both fish had been caught at the same time and at the same place.

The symptoms were typical. About 4 hours after eating the fish there set in severe muscular spasms of the limbs, with cold, clammy extremities, paresis of the muscles of deglutition, dyspnoea, aphonia, burning sensations in the mouth and tongue and cutaneous hyperaesthesia, so that cold drinks and cold baths could not be taken. There was in most a certain degree of shock. Just a year previously, in the same Journal, Feb., 1945, a closely similar outbreak due to the same cause and in the same area was reported [see this *Bulletin*, 1945, v. 42, 592, where a fairly full comment is given]. *H. Harold Scott.*

Menon, I. G. K. **Intestinal Fuso-Spirochaetosis.** *Indian Med. Gaz.* 1945, Sept., v. 80, No. 9, 454–8, 7 figs. on 1 pl.

The author found fusiform bacilli (*Fusiformis fusiformis*) and spirochaetes (*Treponema vincenti*) in the faeces of 16 out of 120 persons examined; notes of clinical and laboratory findings and of treatment are given in the case of four of them and the other twelve are tabulated under the headings clinical condition, cellular exudate, other infections, and spirochaetes. In the four cases described, there were sudden attacks of abdominal pain above the umbilicus and of diarrhoea, lasting for a day or two, or sometimes for a few weeks. Duodenal intubation was done in one patient and spirochaetes and fusiform bacilli were found in the fluid withdrawn. These organisms were present on the gums of all four patients. Of the other 12 patients, 4 had amoebic dysentery and 2 had a history of amoebic infection, 2 had pain and diarrhoea, one had chronic dyspepsia, 1 had upper abdominal pain, and 2 had no symptoms; *Giardia intestinalis* was present in 6. Treatment with stovarsol appeared to cure the symptoms. The possibility that the fusiform bacilli and spirochaetes may cause the symptoms with which they are associated is discussed with references to the work of other authors. *J. F. Corson.*

Toullec, F. La mélioïdose. [**Melioidosis.**] *Les Grandes Endémies Tropicales.* (Onzième Année). 1939. Paris. pp. 49–59.

Webb, A. C. **Primary Carcinoma of the Liver.** *Arch. Pathology.* 1945, Nov.–Dec., v. 40, No. 5, 382–6, 9 figs. [27 refs.]

"A survey of the literature shows that primary carcinoma of the liver is comparatively rare in this country [the United States] and in Europe. The incidence is much higher among some groups of Orientals and Africans.

" To a total of 1,200 cases in the literature 12 cases are added. All the patients were American Negroes. The incidence is seen to be higher in Negroes than in the general population. The data on these additional cases include : age and sex of patient ; type of tumour ; nodularity ; presence or absence of cirrhosis, necrosis, hemorrhage and extrahepatic metastases ; weight of the liver when available.

" In the genesis of the disease the role played by cirrhosis is important.

" Experimental carcinogenesis suggests dietary deficiencies acting as predisposing factors in explanation of the peculiar racial and geographic distribution of the disease."

TAYLOR, C. E. **The Racial Distribution of Nephritis and Hypertension in Panama.** *Amer. J. Path.* 1945, Nov., v. 21, No. 6, 1031–4, 1 fig. [37 refs.]

[Renal disease is one of the most obscure in human pathology and this article forms an interesting pathological study, but leaves the question little, if at all, less obscure.]

For some years it has been known that racial groups living in Panama in close contact and under similar conditions show marked differences in the incidence of hypertension. Thus, it is some seven times as common in the West Indians as in native Panamanians, and in the younger age-groups the proportion might be as high as 16 to 1, as gauged by examination of more than 1,300 persons applying for employment. African negroes under natural, *i.e.* primitive, conditions generally have a relatively low blood-pressure and it is suggested that an important factor in causing the hypertension is " adjustment to a new civilization and a new environment." [This, by itself, is, of course, pure hypothesis.] The author has studied autopsy records for renal changes among 498 cases : 266 West Indian negroes, 77 Panamanians, 135 whites, and 20 " miscellaneous." He presents by way of preliminary a table of histological criteria, dividing the renal changes into three main groups : glomerulo-nephritis (acute, subacute, or chronic), pyelo-nephritis (acute, active chronic, and healed) and nephrosclerosis (arterial and arteriolar) ; a fourth group in which the other three may be combined he designates " unclassified".

Generally, in the whole number of 498, pyelo-nephritis was the most common, nephrosclerosis fairly common, glomerulo-nephritis relatively rare. The numbers in the races examined are so unequal that comparison, except on general lines, is of little value, and as given in percentages the findings are apt to mislead or convey a wrong impression. But, broadly speaking, differences were striking. Thus, among the West Indians, half (49·3 per cent.) had some form of nephritis, more than three times relatively as frequent (15·6 per cent.) as among the Panamanians ; among the whites it was 20·7 per cent. Pyelonephritis was twice as frequent in the West Indians as in the other races ; the arteriolar form of nephrosclerosis was more than seven times as common in the West Indians as among the Panamanians and three times as common as in the whites. Blood-pressure readings were of the same order : West Indians 176/104, whites 159/98, Panamanians 136/89. Sex seemed to play no part in the distribution of renal disease and it is noted that " five per cent. of the negroes and whites had mild hypertension with no evidence of nephritis." The author suggests as an interpretation of this that " essential hypertension " may occur in the whites and the West Indians whereas when hypertension develops in a Panamanian it is probably secondary to renal mischief.

H. Harold Scott.

Bayley, E. C., Lindberg, D. O. N. & Baggenstoss, A. H. **Loeffler's Syndrome. Report of a Case with Pathologic Examination of the Lungs.** *Arch. Pathology.* 1945, Nov.–Dec., v. 40, No. 5, 376–81, 5 figs. [Refs. in footnotes.]

Katzenellenbogen, I. **Behcet's Triple Syndrome. (Report of Three Cases).** *Harefuah.* Jerusalem. 1946, Feb. 15, v. 30, No. 4. [In Hebrew 81–4. (19 refs.) English summary 84.]

See also this *Bulletin*, 1944, v. 41, 780.

Boland, E. W., Headley, N. E. & Hench, P. S. **The Treatment of Agranulocytosis with Penicillin.** *J. Amer. Med. Ass.* 1946, Mar. 2, v. 130, No. 9, 556–9, 1 fig. [Refs. in footnotes.]

"Since 1941 sulfonamides and penicillin have been used in the treatment of granulocytopenia or agranulocytosis. At first they were used more often despite the presence of agranulocytosis rather than specifically for it. Seven cases of agranulocytosis successfully treated with sulfonamides have been reported. But because sulfonamides may themselves produce agranulocytosis, penicillin would seem to be the remedy of choice.

"Ten cases of agranulocytosis, including the one here reported, have now been treated with penicillin: prompt recovery has occurred in every case. This represents a notable improvement in the treatment of the condition and allows for much greater optimism in prognosis than has heretofore been possible. In some of these 10 cases leukopoietic agents were used in conjunction with penicillin, but the current trend is to rely on penicillin alone. Experiences to date indicate that penicillin constitutes the most potent remedy at hand for the prevention or control of the serious, potentially fatal complication of agranulocytosis.

"Since this paper was submitted for publication another case of agranulocytosis successfully treated by penicillin has been reported. Thiouracil had been given for hyperthyroidism; the leukocyte count fell to 2,400 with 2 band cells and 2 segmented neutrophils. Treatment included a transfusion, liver extract and a total dose of 560,000 units of penicillin in four days, after which recovery was complete."

Kean, B. H., Tucker, H. A. & Miller, W. C. **Ainhum: a Clinical Summary of Forty-Five Cases on the Isthmus of Panama.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 331–4.

In the 40 years ending May 1944, 45 cases of ainhum have been traced in Panama; this number represents 1·5 per 10,000 West Indian male admissions to hospital. All the ainhum patients were West Indians, 20 from Jamaica, 10 from Barbados; they were all males and none was white or half-caste. Thirteen were between 21 and 30 years of age at the onset of the disease, 11 between 41 and 50; 8 between 31 and 40. Six had the condition before coming to Panama, and in two-thirds of the cases just over 11 years elapsed between arrival in the district and onset of symptoms. The little toes were involved in all; both sides in 14, the right alone in 18, the left alone in thirteen. In one patient the third and fourth toes were affected, also on both sides. In one only was there a family history, the father having been similarly afflicted.

Pain was marked, in fact the chief symptom for which hospital relief was sought. A history of local trauma was elicited in 4 only. No evidence was obtained of any aetiological connexion between ainhum and leprosy, syphilis, scleroderma or arteriosclerosis, and the author postulates "hereditary racial tendency" as the main factor [which, if it has any meaning at all, is purely hypothetical.] *H. Harold Scott.*

Tye, M. **Ainhum.** *New England J. of Med.* 1946, Jan. 31, v. 234, No. 5, 152–4, 2 figs. [24 refs.]

" The first case from New England of ainhum, or spontaneous dactylolysis, is reported. The results of pathological study and the roentgenologic findings are reported, and the literature is reviewed."

GENERAL ENTOMOLOGY.

Dethier, V. G. **The Transport of Insects in Aircraft.** *J. Econom. Entom.* 1945, Oct., v. 38, No. 5, 528–31.

From December 1943 to April 1945, 816 collections of insects were made in aircraft flying between India and the west coast of Africa. The author groups the 2,006 insects collected into 86 families and 13 orders. The order Diptera constituted 88·5 per cent. of the total catch, and one species, *Musca sorbens*, accounted for 45·9 per cent. of all insects caught. Only ten mosquitoes were taken, owing to precautions observed at the airfields. There were some *Simulium griseicollis* between December and February in the Sudan, but no *Phlebotomus* during the sandfly season March to September.

The insects gain entry to the cabin when the aircraft is grounded ; they either fly in or are carried in on passengers or cargo. There is no evidence that they enter during flight of the aircraft. No insects were found in the engine nacelles and the only species taken from dismantled or wrecked wing and tail spaces was *Musca sorbens*.

One hundred tests were made with caged *Anopheles gambiae* placed in the nacelles for flights ranging from fifteen minutes to four hours' duration. In 99 instances all mosquitoes were dead after the flight and in one test they were so battered that they died soon after removal. Other tests showed that insects in the nacelles were killed during the take-off.

The author concludes that effective precautions taken on air fields reduced the number of insects entering the aircraft, and that along the route studied insect control in the aircraft themselves is necessary in the cabins only.

H. S. Leeson.

Beament, J. W. L. **Waterproofing Mechanism of an Insect Egg.** [Correspondence.] *Nature.* 1946, Mar. 23, 370.

Webb, J. E. **The Penetration of Derris through the Spiracles and Cuticle of *Melophagus ovinus*, L.** *Bull. Entom. Res.* 1945, July, v. 36, Pt. 1, 15–22, 1 fig. [16 refs.]

" In *Melophagus ovinus*, derris dust is shown to be absorbed through the spiracles and tracheal system. The amount of dust entering the tracheae is governed by the structure of the inspiratory spiracles and the rate of flow of the inspired air.

" Factors stimulating the rate of respiration of the insect—*i.e.*, increased muscular activity, the presence of 5 per cent. carbon dioxide and a rise in temperature, increase the rate of entry of derris into the body.

" Penetration of derris takes place slowly through the external cuticle at 30°C., but not at all at 20°C. It is postulated that the entry of derris through the cuticle probably depends on the hardness of the lipoid layer."

Webb, J. E. & Green, R. A. **On the Penetration of Insecticides through the Insect Cuticle.** *J. Exper. Biol.* 1945, Dec., v. 22, Nos. 1/2, 8–20, 2 figs.

Some previous observations showed that certain insecticides, *e.g.*, Derris, were more effective in the presence of solvents such as high boiling tar acids.

Since it seemed likely that the solvents acted by facilitating penetration, an investigation into this possibility was undertaken.

Diphenylamine was chosen as the insecticide, since it is soluble in a wide variety of organic solvents. It was first mixed with kaolin, and 1 per cent. by weight of the solvent was then added.

The sheep ked, *Melophagus ovinus*, was used as the test insect. Groups of five keds in corked specimen tubes received liberal doses of insecticide and were later examined for cessation of heart beat. In a previous paper by Webb [above] it was shown that derris dust entered the spiracles ; in the present instance, however, such entry is negligible and the diphenylamine acts after absorption through the cuticle.

It was found that only certain solvents of diphenylamine increased the rate of action ; *e.g.*, cresols, benzyl alcohol and 4-methyl-cyclohexanol. Other solvents, for example carbitol and methyl benzoate, did not produce this effect. The capacity of a solvent to induce rapid action is described as its " carrier efficiency."

It is suggested that the cuticle covering an insect may be thought of simply as a two phase system, comprising an outer phase of lipophilic elements associated with the epicuticle, and an inner phase of hydrophilic elements associated with the exocuticle and endocuticle, which is traversed by lipophilic elements. If this concept of the cuticle structure is accepted, it can be seen that in order to reach the hypodermal cells below the cuticle, the penetrating substance must traverse first a lipophilic and then a hydrophilic layer. Measurements were made of the rate of passage of solvents through beeswax (taken to represent the lipophilic layer), the solubility of the solvents in water the partition coefficients of the solvents between beeswax and water, the solubility of the diphenylamine in aqueous solutions of the solvents, and the volatility of the solvents. It was concluded that a high carrier efficiency could be correlated with a high rate of penetration through beeswax, a high partition coefficient of the solvent between beeswax and water, and a high solubility of insecticide in a solution of the solvent in water. The volatility of the solvent, and the solubility of the insecticide in it, were also relevant factors.

As a result of the above observations it is suggested that solvents which facilitate penetration do so by transporting the insecticide across the lipoid elements of the epicuticle to the interface between this layer and the water of the exocuticle. They also concentrate the insecticide in the epicuticle/exocuticle interface and so by raising the concentration there increase the diffusion gradient. Finally the solvents diffuse into the exo- and endocuticle and raise the partition coefficient between the solvent in the epicuticle and the water in the exocuticle.

Mixtures of two solvents each deficient in some of the above properties, but together possessing all the essential physical properties, showed a carrier efficiency higher than that of either constituent alone.

Besides diphenylamine the results were shown to apply to dixanthogen, ω-nitrostyrene dibromide and rotenone, but it does not necessarily follow that the carrier efficiency of a solvent is the same for all insecticides.

W. A. L. David.

Kumm, H. W., Osborno-Mesa, E. & Boshell-Manrique, J. **Studies on Mosquitoes of the Genus *Haemagogus* in Colombia (Diptera, Culicidae).** *Amer. J. Hyg.* 1946, Jan., v. 43, No. 1, 13–28, 1 fig. & 6 pls. (1 coloured). [21 refs.]

" 1. Eight species of *Haemagogus* were found in Colombia, 7 of them in the lowlands and one in the highlands.

" 2. The commonest and most widely distributed species was *Haemagogus spegazzinii falco.*

" 3. In South America there appear to be several species and subspecies of *Haemagogus* with hairy larvae, the males of which can be distinguished one from another by the morphology of the mesosome in its lateral aspect.

" 4. The name *Haemagogus spegazzinii* subspecies *falco* is proposed for the Colombian form, which has been incriminated repeatedly as a vector of jungle yellow fever.

" 5. Keys and diagrams are given for separating the larvae, adults and male terminalia of the *Haemagogus* of Colombia."

PAGE, A. B. P., STRINGER, A. & BLACKITH, R. E. **Investigation of Insecticidal Sprays.** *Nature.* 1946, Jan. 19, 80–81, 2 figs.

The authors have developed a method of determining the amount of insecticide picked up by insects flying through insecticidal sprays. Aluminium chloride is added to the spray (which is necessarily an aqueous emulsion) and the amount in washings from 100 insects is determined colorimetrically by means of the blue lake formed in a buffered solution with haematoxylin.

Experiments with various concentrations of pyrethrins and different spray dosages have shown that a very small quantity of pyrethrins picked up (about $0{\cdot}12 \times 10^{-7}$ mgm. per mosquito) causes the mosquito *Aëdes aegypti* to become abnormally active. This increases the rate of spray pick-up until the amount of pyrethrins acquired reaches about $6{\cdot}0 \times 10^{-7}$ mgm., when the insect is knocked down. This quantity of pyrethrins per insect, effective in causing knock-down, is the same at all spray dosages (it is about 1·25 mgm. per kgm. body weight). The efficiency ratio (effective dosage/nominal dosage) varies, however, decreasing rapidly as the dosage of spray is reduced from 10 to 35 ml. per 100 cu. m. The various relationships between pick-up, concentration of pyrethrum and spray dosage are illustrated graphically. It is also shown that, with aqueous pyrethrum sprays, the efficiency ratio is lowered as the humidity of the chamber is reduced. *J. R. Busvine.*

EIDE, P. M., DEONIER, C. C. & BURRELL, R. W. **DDT as a Culicine Larvicide.** *J. Econom. Entom.* 1945, Oct., v. 38, No. 5, 537–41.

It has previously been shown [DEONIER *et al.*, this *Bulletin*, 1946, v. 43, 101] that DDT is an outstanding anopheline larvicide. The present paper describes tests on culicine larvae carried out with preparations of DDT in the form of dusts, suspensions, or surface films in various solvents.

The tests with domestic culicine species were carried out in rain barrels of 55 gallon capacity, sawn in half, which were infested naturally from a nearby stock tub containing water and horse manure. The toxicity was estimated by dipping and by introducing larvae.

Field tests were also made, and dips were taken to estimate the number of larvae present. The DDT was dusted, poured or sprayed on in various ways.

Dusts and suspensions of DDT and phenothiazine were compared in barrels, mainly against *Culex quinquefasciatus* [*C. fatigans*]. It was concluded that DDT is more toxic than phenothiazine ; dusts are not so effective as suspensions ; as a dust DDT is far superior to phenothiazine ; both DDT and phenothiazine are effective for long periods when applied in heavy dosages.

DDT applied as a 10 per cent. suspension with " Cellosolve " and " Nopco 1216 " was slightly more effective than DDT in xylene emulsified with " Triton x-100." In the latter case the quantity of emulsifer used did not seem to have an appreciable effect on toxicity. In suspensions 1 p.p.m. showed residual toxicity to species breeding in rain barrels.

In the field, tests were made against salt and fresh water species. Suspensions and emulsions of DDT were more effective than surface applications in dusts or oils, and control was obtained in places which could not be reached with ordinary larvicidal oils.

Many of the culicine species are more resistant than anophelines to DDT, but effective, though not complete, control of the following species was obtained with only 0·05 p.p.m. *Aëdes taeniorhynchus, A. sollicitans, A. aegypti, Psorophora confinnis, P. ciliata, Culex quinquefasciatus* [=*C. fatigans*], *C. pilosus, C. nigripalpus* and *C. salinarius.* At 1 p.p.m. of DDT as suspension, a residual toxicity lasting for five weeks was obtained. However, at high concentrations, DDT affects other aquatic animals.

In comparison with the above, petroleum oil solutions of DDT (1–5 per cent.) applied as surface films gave 100 per cent. control at about 0·1 lb. or more of DDT per acre, in ponds filled with vegetation. Lower doses showed incomplete control. Fuel oil alone at 1·2 gall. per acre gave 0–85 per cent. reduction of larvae, depending on the vegetation present. *W. A. L. David.*

Magy, H. I. & Hoskins, W. M. **Some Dinitrophenol Derivatives as Mosquito Larvicides.** *J. Econom. Entom.* 1945, Oct., v. 38, No. 5, 524–7, 1 fig.

This paper presents a more detailed investigation into the larvicidal efficiency of the dinitrophenol group of compounds than has hitherto been available. It was known previously [Campbell *et al.*, this *Bulletin*, 1935, v. 32, 663] that 3,5 dinitro-*o*-cresol was toxic to culicine larvae at 1 : 10,000, some of the material being present in suspension. The importance of the suspended material is now demonstrated.

The three compounds tested were :—3,5 dinitro-*o*-cresol (DNOC), 2,4 dinitro-*o*-cyclohexyl phenol (DNOCHP) and the dicyclohexyl amine salt of the latter compound (DCA-DNOCHP). The materials were used in solution or precipitated from strong acetone solution just before the larvae were introduced. Under such circumstances solution was slow. The small quantity of acetone was without effect on the larvae. The *p*H values of the waters used were examined, since in alkaline media these compounds go into solution as salts. The *p*H of the larval gut was also tested with indicators and found to be alkaline in the anterior portions.

Of the three compounds, DNOC was least toxic in solution and at 140 mgm. per litre it produced a negligible kill of *Culiseta incidens* fourth stage larvae in 48 hours ; in comparable tests the other two compounds produced a 50 per cent. kill at about 70 mgm. per litre. In contrast with these results,when the solution contained suspended undissolved material, the toxicity was much higher. For example, a solution of 82 mgm. per litre of DNOCHP, which contained in addition 7·5 mgm. per litre in suspension, gave a 100 per cent. kill in two hours. DNOC was too soluble to form a satisfactory suspension. It was concluded that these dinitro compounds have little contact toxicity, but that they function as stomach poisons.

Field tests with the materials applied as dusts on a weedy ditch showed high kills of *Anopheles maculipennis* with dusts containing 10 per cent. DNOCHP or 40 per cent. DCA-DNOCHP, each applied at the rate of 50 lb. to the acre. The latter dust was less toxic to other aquatic life. *W. A. L. David.*

Parrot, L. & Martin, R. Notes sur les phlébotomes. XLIX. Autres phlébotomes du Moyen Congo. [*Phlebotomus* **of the Middle Congo.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Dec., v. 23, No. 4, 279–80, 1 fig.

Parrot, L., Mornet, P. & Cadenat, J. Notes sur les phlébotomes. L. Phlébotomes de l'Afrique Occidentale Française. 2. Guinée, Côte d'Ivoire, Dahomey. [*Phlebotomus* **of French West Africa : Guinea, Ivory Coast, Dahomey.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Dec., v. 23, No. 4, 281–9, 8 figs.

Latyshev, N. I. [**Instructions for testing of Sandfly Repellents.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 82–5. [In Russian.]

The author points out that very little is known regarding chemical methods of protection against sandflies, and discusses the methods of testing repellents and the results of some tests with sandflies. Observations on the efficacy of the repellents can be carried out by applying the chemical (1) to one side of the face or to one arm while leaving the opposite side of the face or the other arm untreated ; (2) to one individual and using a second one as control ; (3) to one part of a window leaving the other free ; (4) to whole groups of people with adequate controls. In the case of (1–3) the repellent effect is determined by comparative counts of sandflies, while in (4) it is assessed on the basis of evidence of bites.

The following repellents have already been successfully used against sandflies : (1) bis-ethylxanthogen (Preparation " K " : see also this *Bulletin*, 1945, v. 42, 940) used as a 3–5 per cent. solution in vaseline ; (2) 3 drops each of anise oil, eucalyptus oil and turpentine, lanolin 30 gm. ; (3) turpentine 10 parts, tar 4 ; Dalmatian powder and castor oil, 20 of each ; lanolin and vaseline, 40 of each ; (4) Japanese menthol 1 part, dilute carbolic acid 2, vaseline 100.

Good results against other blood-sucking Diptera were obtained with wide-meshed nets impregnated with one of the following repellents and worn on the head : (1) lysol 30 parts, turpentine 10, vegetable oil 5, water 55 ; (2) 5 per cent. solution of caustic potash to which 10 per cent. of tar is added. It is suggested that the effect of these repellents on sandflies should also be tested.

C. A. Hoare.

Delmanto, A. Sôbre a miíase oftálmica. Tratamento de sua localização intra-orbitária. [**Myiasis of the Eye : Treatment.**] *Publicações Medicas.* São Paulo. 1945, Aug., v. 17, No. 1, pp. 17, 19–21, 23–4, 2 figs.

Mac Arthur, W. P. **Habituation of *Pulex irritans* to Animal Host.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 343–4.

The author relates a personal observation which showed that *Pulex irritans* may become adapted to live on a dog. His spaniel was accidentally found to be infested with this species of flea, 100 being recovered from it ; he had the dog on his knees and carried it in his arms but no fleas passed from the dog to infest him though he is ordinarily attractive to fleas. The fleas were removed from the dog in an unoccupied room and some escaped ; when the author entered the room, purposely lightly clad and four days afterwards, the fleas bit him viciously. A few fleas were found on the dog for over a year in spite of all measures taken to rid it and the house of them. None of the other five occupants of the house was bitten.

On other occasions, when collecting fleas from dogs and cats, the author has found more *P. irritans* than *Ctenocephalides canis* or *felis*, *e.g.*, in the proportion of 20+ to 2 and 9 to 3.

This experience leads him to think that in former times, in Europe, *P. irritans* may have become habituated to the house rat and may have helped to spread plague from rats to man.

J. F. Corson.

SERGENT, E., DONATIEN, A. & PARROT, L. Expériences de protection des animaux domestiques contre la piqure des tiques par la poudre insecticide D.D.T. [**The Protection of Domestic Animals against Ticks, by DDT.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Dec., v. 23, No. 4, 249–59, 4 figs.

LABORATORY PROCEDURES.

LILLIE, R. D. **Effect of Metals on Giemsa Stain Solutions in Fifty per cent. Glycerol and Methanol Mixture.** *J. Lab. & Clin. Med.* 1946, Feb., v. 31, No. 2, 253–6.

During the recent world war a batch of Giemsa stain solution deteriorated after the bottles had been issued to various places, the eosin staining being lost. The bottles had screw caps lined with tin foil seals and these were noticed to have a yellow incrustation. The tin foil was later found to consist of tin (99·7 per cent.) with small amounts of lead, copper, arsenic, antimony and iron. Experiments were made with the tin foil and with various metals to see what effect they had on Giemsa stain solution as indicated by spectroscopic examination. The results are given in tables ; it was found that various metals, "relatively active in the electrolytic series," decompose thiazine eosinates in glycerol methanol solution [Giemsa's stain] and remove eosin from the solutions. Alkali earth metals appear to act purely as alkalies. Zinc acts on methyl thionins but not on thionin.

The authors conclude that tin foil or other foils containing tin, zinc or cadmium should not be used for lining screw caps for Giemsa's stain ; paraffined cardboard is satisfactory for the purpose. *J. F. Corson.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

MEGAW, J. **The Health of India.** *Brit. Med. J.* 1946, Mar. 9, 343–7.

This appraisement of the health of India by a recognized authority is concerned, almost exclusively, with the practically universal malnutrition caused by insufficient and unsuitable food. In countries in which malnutrition and infectious diseases have been reasonably well controlled, the average length of life has increased to well over 55 years. In India, where much has been done to control infectious disease but little or nothing to tackle the malnutrition problem, the average length of life is but half this figure. The control of epidemics has contributed to a prodigious increase in the rate of growth of the population. Between 1931 and 1941 the increase of population for the whole of India was 15 per cent., an actual increase of about 50,000,000. In parts of India the increase attained 22 per cent. " The people must choose for themselves whether to adhere to the present system of unrestricted propagation of children with its attendant misery or voluntarily to apply an adequate check." The magnitude of the problem as set forth is staggering, and this lecture was delivered before the imminence of widespread famine that faces India today was recognized. Increase in the production of food can scarcely keep pace with population increase unless drastic changes are made in outlook of life and manner of living. The abolition of uneconomic small-holdings, and the elimination of millions of useless cattle, would be fiercely resisted.

The creation of a Commission is urged, to make an unbiased report on social and other customs which cause ill-health and economic depression in the rural population, and to recommend suitable action to effect a change. The Commission should consist of enlightened Indians, especially Indian women. Such a Commission might create a sense of danger needed to convince the people of the need for a change in their plan of life. *Norman White.*

WOOLLEY, E. J. S. **The Health of the Civilian Population of Tristan da Cunha.** *J. Roy. Nav. Med. Serv.* 1946, Jan., v. 32, No. 1, 3–15, 7 figs.

Tristan da Cunha is no longer the *terra incognita* it was at the beginning of the century, but this account is interesting in bringing information concerning the island up to date. The settlement has been in existence for 130 years, and the population in 1944 was 122. Registers of marriages and births have been kept since 1871 and 1880, respectively, and of deaths since 1892. The types of inhabitants range from " whites ", with fair hair and blue eyes, to dark mulatto. The adults are of good physique, the children and adolescents are not ; this is ascribed to deterioration in the standards of living, for since there is less trade with passing ships, the people have to depend more on their own efforts and the crops consist almost entirely of potatoes ; this food being supplemented by pumpkins, fish and a few eggs of sea-birds and fowls. Of late years there has been a little grazing, and consequently a little milk-production. The island has no alcoholic drink. Living conditions are still primitive—houses of stone roofed with New Zealand flax or tussock grass ; sanitation is hardly existent. If buckets are used, they are neglected as soon as they are full, or are emptied in heaps near the dwellings.

Epidemics of colds and tonsillitis occur, but there are no authentic records of any other epidemics, if we except outbreaks of mild enteritis in the summer months when flies are a pest. Many suffer from local sores, whitlows, boils, cellulitis, impetigo, which heal with difficulty and slowly. *Ascaris lumbricoides* is found to infest almost the entire population. The commonest disease is asthma (97 cases), next is fibrositis (18) and dyspepsia (11). In spite of the severity of the common cold, pulmonary disease is rare. Labour is usually easy and maternal mortality is nil ; children are breast-fed for a year or so, but after 4 months they are given, in addition, potato, and the infants are undersized, anaemic and dyspeptic. Hereditary deformities are noted ; nine descendants of one woman show deformity of the pinna, with partial or complete meatal occlusion ; others showed polydactyly and " lobster hand ". Intelligence is not easy to gauge, because of the isolation of these people, but 152 are said to be " normal ", able to support themselves and their families and to be educationally receptive ; 43 are " dullards ", feckless, improvident, lazy and lacking in initiative, but capable of working under supervision ; nine are " high grade defectives." [This account of the general state and mode of life of these islanders makes gloomy reading—a marked contrast with the happy, healthy lives of the early inhabitants of the former lonely Pacific island, Pitcairn.] *H. Harold Scott.*

BLANCHARD, M. Quelques particularités de la pathologie de Madagascar. [**Remarks on Disease in Madagascar.**] *Les Grandes Endémies Tropicales.* (Onzième Année.) 1939. Paris. pp. 5–13.

This is of the nature of a farewell talk by Inspector-General Blanchard. In it he refers in a few words to each of the following subjects : Plague, yellow fever, trypanosomiasis, smallpox, and typhus in a group of infectious diseases. The chief point to note in this group is the possibility of introduction of yellow

fever. The author does not think that infective *Aëdes* are likely to be brought in, and the chief danger is from persons in the incubation or early stage of the disease. A second group he mentions is that of endemic diseases, and here he refers briefly to malaria, syphilis, tuberculosis, leprosy, beriberi and rabies. The proposal has been made to decentralize large leprosaria and collect or re-group the inmates in small villages of 6 to 30 patients near medical centres and near their own homes. Other conditions briefly referred to in this paper are uratic deposits, alcoholism, intoxication by *Cannabis indica*, the last of which is becoming more common as the price of tobacco rises. The only surgical condition spoken of is bites by caymans and in this connexion he cites a case which occurred in 1938. [The article is interestingly written, but consists in the main of general remarks, nothing new being contributed; there are many things one would expect to find mentioned, but they are not even referred to, such as the use of the living E.V. strain of *P. pestis* in prophylaxis in Madagascar.] *H. Harold Scott.*

DAVID, J. Une oeuvre française aux îles Wallis et Futuna. [**French Work in the Islands of Wallis and Futuna.**] *Les Grandes Endémies Tropicales.* (Onzième Année). 1939. Paris. pp. 72–92.

VAUCEL. L'aspect social de la médecine aux Colonies. [**The Social Aspect of Medicine in the French Colonies.**] *Arch. Méd. Sociale.* Paris. 1945, Aug., v. 1, No. 5, 325–8.

The author makes the point that, in the colonies, medicine is social in so far as it copes with diseases which are widespread, and that for this purpose campaigns on a large scale are deliberately planned. [This recalls the remark made in Lord HAILEY'S *An African Survey*, that "disease of the type which causes most mischief in Africa is generally a mass infliction, and must be attacked in the mass." See this *Bulletin*, 1938, v. 35, 934.] Instances of this kind of campaign are given. The sleeping sickness treatment services in West Africa, examine 6,000,000 persons each year, among whom about 20,000 cases of sleeping sickness are discovered annually. The epidemic has been stabilized and the infection rate is now about 0·5 per cent. For the prevention of yellow fever, more than 10 million people have been vaccinated by the scarification method. In Madagascar extensive use has been made of the live E.V. vaccine; in 10 years five million people have been vaccinated, and the incidence of plague has fallen from 3,584 cases in 1934 to 184 in 1944.

The author writes in general terms on the provision of a service of travelling units for the discovery, treatment and prevention of the major diseases, which should achieve a standard of efficiency much greater than is possible under the present system of fixed dispensaries. *Charles Wilcocks.*

DE BRIEY, P. **Migration of Indigenous Workers in the Belgian Congo.** *Internat. Labour Rev.* 1945, Oct., v. 52, No. 4, 335–51. [Refs. in footnotes.]

In an earlier paper, Dr. Margaret READ discussed the effect of the migration of African males from Nyasaland, in search of work, upon the communities left behind [this *Bulletin*, 1942, v. 39, 723]. In the present paper, de Briey discusses the same problem and the regulations formulated to deal with it, in the Belgian Congo. The least harmful form of migration is the seasonal search for work, when the men take employment for a short time only away from their homes. In this form there is relatively little interference with village economy, and the men retain a strong connexion with their own communities. Much more serious in its effect on the men and on their families, is the migration for work which entails absence from home lasting for 3 years or so, especially if

the place of work is far from the village. Under these circumstances the men are suddenly placed in unfamiliar surroundings, to which they may react badly for themselves and their people. The age and sex balances of the villages are seriously disturbed if many men are away for long periods. The situation is less harmful if the place of work is near the homes of the workers.

The treatment of men detached from their home surroundings must obviously be considered with special care, more especially if they have been recruited for work under conditions of which they have no exact understanding ; there are, therefore, special regulations governing the recruitment of labour. In the Belgian Congo measures have been taken to protect both the indigenous community and the indigenous worker. For the community from which the workers are drawn there is a land policy by means of which the Government tries to prevent the complete exhaustion of the labour supply in some areas by directing settlers from Belgium to areas where manpower is plentiful. There is also a social policy. The governor of a province may prohibit all recruitment of Africans if recruitment would mean that an undue proportion of men (over 10 per cent. of able-bodied men, that is, over 2·5 per cent. of the whole community) were removed from the district. Reduction of the male population beyond this figure entails risk to the health, and even to the continued existence, of the community. In formulating this principle the Government have taken into account that spontaneous application for employment does occur among the Africans, and that the number of persons thus actively seeking work is considerable. It is impossible to prevent those Africans from going to work who, of their own accord, show that they wish to contract an engagement ; the restrictions, therefore, apply only to active recruitment.

It is realized that if large concessions are made to Europeans in some areas, the attractions offered to the Africans may be so great as to tempt away the whole male population from their homes. This would, however, not necessarily be so disastrous as recruitment, because experience has shown that under some conditions the family of the African would accompany him. Nevertheless, the social consequences would be serious unless adequate steps were taken to provide for the welfare of these families in their change to a new life. " It is precisely the function of a colonial Government to create economic conditions tending to give the indigenous population a stable social environment adjusted to its degree of development." Attempts are therefore made by companies to stabilize the indigenous workers in their new surroundings, by favouring long-term engagements and by providing for the health and well-being of the workers. Periodical wage increments and bonuses for married men and those with children offer inducement to stay and to bring wives and families. Medical services are provided, in one case costing 10 per cent. of the total cost of indigenous labour employed. Education is also provided, and social institutions which cover a wide range of activities are encouraged. These efforts have been successful in creating new and stable communities. Stabilization will not abolish the evils which may attend the process of turning the tribal Africans into an industrial proletariat, but it will make them smaller.

The author concludes with the remark that whatever measures the Government adopts to deal with this complex problem, success will depend on the human factor. [The line of thought that runs through this paper is very similar to that propounded by Sicé (this *Bulletin*, 1946, v. 43, 257). The medical reader may draw the conclusion that since the impact of industry on the African will affect both his physical and mental health, it is the duty of Governments to seek the advice of their medical officers, much more than has in the past been the case, as to the measures to be adopted, and that the purely commercial point of view should not be given the priority it has too long enjoyed.] *Charles Wilcocks.*

WRIGHT-SMITH, R. J. **A Case of Fatal Stabbing by a Stingray.** *Med. J. Australia.* 1945, Dec. 22, v. 2, No. 25, 466–7, 2 figs.

G. P. WHITLEY, in his work on *The Fishes of Australia*, describes six varieties of stingray in Victorian waters. The spine is strong and can be driven through the side of a boat and the fish can show great accuracy in stabbing. They often come into shallow waters for warmth and lie in the sands.

The case here recorded is that of a man of 33 years, a powerful swimmer, who, when coming in from a bathe, suddenly showed symptoms of distress ; he was helped in by friends and was breathing with difficulty ; 20 minutes later he died. There was an oval-shaped stab wound, ½-inch long, at the fifth left intercostal space found at autopsy to have penetrated the pleural cavity and the pericardium, and there was an irregular tear of the left ventricle, 3/8th-inch in length, near the apex. There was a smaller wound, not penetrating beyond the subcutaneous tissue, on the mesial side of the first. The pericardial sac was found to contain fluid blood and there was much blood and some clot in the pleural sac, and haemorrhage round the wound in the left ventricle. The organs generally were healthy. The palings of the fence round the bathing place were broken and the stingray may have thus gained entrance. The water was dirty and nothing could be seen on the sea-bed ; no weapon, spike or nail was found which might have caused the injury [but nor was any stingray].

H. Harold Scott.

BULL. HEALTH ORGANISATION. (League of Nations). 1945/46, v. 12, No. 1, 111–79. **The Unification of Pharmacopoeias. Interim Report of the Technical Commission of Pharmacopoeial Experts. (May 1945.)**

BOOK REVIEWS.

Manson's Tropical Diseases. A Manual of the Diseases of Warm Climates.—Edited by Philip H. MANSON-BAHR, C.M.G., D.S.O., M.A., M.D., D.T.M. & H. Cantab., F.R.C.P. London, Senior Physician to the Hospital for Tropical Diseases, London, etc. Twelfth Edition.—pp. xiv+1068, 17 colour pls., 9 half-tone pls., 407 text figs., 6 maps & 29 charts. 1945. London, Toronto, Melbourne & Sydney : Cassell & Co., Ltd. [42*s.*]

Manson's Tropical Diseases, under the able and indefatigable editorship of Sir Philip Manson-Bahr, goes from strength to strength. In the five years since the eleventh edition was issued there have been momentous happenings ; hundreds of medical men have been serving in the tropics for the first time and have met with diseases new to them, and differences in diseases with which they were familiar in temperate climates. These have rushed eagerly into print to record their experiences, and the result has been a spate of literature, some of it of value, but much of it everyday matters to readers of this *Bulletin*, with their extensive tropical experience. Also, the fact of having large numbers of men fresh to tropical conditions under their care has afforded a unique opportunity for the more experienced to carry out research in the field on a large scale and to apply measures already tested and found successful in the laboratory. To sift all this vast amount of material, to separate the wheat from the chaff and present the wheat in a palatable and assimilable form has been the self-imposed task of the Editor, and admirably has he performed it. He acknowledges freely and fully the help he has received from the Bureau of Hygiene and Tropical Diseases and its *Bulletin*, and from the annual summaries of the previous year's

progress in all the important tropical diseases, which epitomize the abstracts made in the *Tropical Diseases Bulletin* on the several subjects during that year.

There is hardly need to review in full a work of such popularity as this. Its usefulness is obvious in the fact that a new edition has been called for every 4–5 years since it first saw the light and that, in addition, it has been reprinted no less than 17 times. Since the last edition was published in 1940 several matters which were then *sub judice* or obscure have been decided or solved, necessitating modification in presentment. Suggestions then put forward for the consideration of the Editor have been carefully weighed and a number of them adopted.

In view of the developments in tropical medicine which have taken place in these five momentous years in the history of medicine, and in particular of tropical medicine, the Editor has found it necessary to recast some sections and to re-write others afresh, to re-draw some of the illustrations and add new ones ; nevertheless, so ably has this been accomplished that though there are 43 more text-figures, the whole book is 15 pages shorter than the 11th edition. New matter which is exceptionally welcome includes a chapter on the Technique of Injections and Blood-transfusion, and a list of special drugs used in the treatment of tropical disease, nay more than a list, for in the case of each we are given its common synonyms, its chemical constitution and formula, its therapeutic application and dosage. This is, indeed, a boon ; but the section will need constant revision as new drugs are introduced, some to replace old ones which will drop out, others to serve new ends.

To pass to matters of detail : There are signs on almost every page of most careful revision, even to cutting out of single words to save space, if the sense is not endangered thereby. Again, by printing two lines more on a page more space has been gained, so that the new edition, with more letterpress, has even fewer pages than the last. This edition has 7 plates fewer than the preceding ; we are sorry to miss the one depicting alastrim and that of the macular rash of leprosy. Whether it was wise to reproduce plates on both sides of a leaf is perhaps a matter of opinion, but the saving of less than half a score of pages is hardly compensated by placing some illustrations right away from their context, as, for example, inserting the beautiful coloured plate of dysenteric lesions of the intestine in the pellagra section. The two pellagra plates could have been placed together and the dysentery one separate, instead of one pellagra plate by itself and the other with the dysentery plate. Again, the radiograph of calcified cysticerci comes in the guinea-worm section.

The part dealing with Food is a good summary of a difficult subject. Tropical anaemias are interestingly described, but one fails to find reference to the pallor wrongly spoken of as tropical anaemia, where there is no true anaemia. The risk of cooling drinks by addition of ice is not mentioned, though it is often done and may be a very serious risk. There is a peculiar slip on p. 29, which might be designated an accident of accidence, and another on p. 117, where γ is said to be equal to 0·0001 gm. γ = one-millionth of a gramme, or 0·001 mgm. On p. 105, in Fig. 145, the male and female *W. bancrofti* have been transposed ; the formula of thiobismol (p. 52) needs a little correction.

The malaria section is one of those which have practically been re written ; that on yellow fever is another. The list of malaria vectors has been both revised and much enlarged and there is also included a list of the regions of their typical breeding-places. The typhus table has been remodelled and brought up to date ; the text here has been to a great extent re-written and now includes Lone-star (Bullis) fever, and the account of the Q fever of Queensland is much fuller. The vitamin chapter has been expanded and almost entirely re-written. The inclusion of a table of syndromes characterized by glossitis and stomatitis was a happy thought. Other useful additions to which special attention should be directed are the improvement of the *Glossina* table by

accompanying drawings of their distinguishing characteristics ; most informative also is the summary of the present state of trypanosomiasis in different parts of Africa ; a short section on tick-borne encephalitis has been added (p. 618). A very valuable addition is the section on Technique of Injections, Blood-transfusions, etc., already alluded to. This is separate from the one on Laboratory Technique, staining methods, etc., usually included under the term Clinical Pathology.

May we, with all deference, offer a suggestion or two for the Editor's consideration ? It is a little difficult to understand the reason for including forms of anaemia, gonorrhoea, diabetes, pulmonary tuberculosis, gout, zymotic diseases, goitre and malignant growths in a chapter on Life in the Tropics. The forms of anaemia met with are important enough to warrant a separate chapter and we venture to suggest that the two excellent opening chapters might end at the middle of p. 30 and a third introductory chapter be inserted on " General Diseases of Temperate Climates as modified in the Tropics." Next, mention might be made of paralytic accidents in the treatment of rabies ; more stress might be laid on the differences rather than on the similarities between tropical eosinophilia and Loeffler's syndrome ; the risk of confusing the Lentz bodies of distemper in dogs with the Negri bodies of rabies—and the so-called hysterical form of distemper may resemble rabies—and hence dispensing with inoculation for determining the diagnosis of the latter ; the use of carbolic (Lifebuoy) soap emulsion, obtainable almost anywhere, in delaying the action of snake venom and so enabling time to be gained for obtaining the necessary antivenene. Lastly, the Appendix, Section A, should be designated Medical Zoology, because it includes three subsections, Protozoology, Helminthology, and Entomology. As it is, the whole section is named Medical Protozoology, which incidentally has been rearranged, and in it are included the two latter. The designation was better in this respect in the previous edition.

In conclusion, those who possess the eleventh edition are strongly advised to purchase this, the twelfth, because it is almost a new work, for the changes are many and important and no one who intends to keep up with the times can afford to be without it. Also, now that men are returning from service abroad, a proportion of them suffering from, or harbouring the seeds of, tropical disease, the general practitioner at home can no longer take up the attitude that such diseases do not interest him and are beyond his purview, and he, too, should read this book with care and keep it on his shelf.

To review the new " Manson " has been a privilege, a πόνος ἄπονος—a true labour of love—and the Editor is to be heartily congratulated on the successful accomplishment of a Herculean task. " Manson " remains the best one-volume work on tropical medicine in English and probably in any language.

H. Harold Scott.

Pereira, O. de Loiola. **Contribuição ao Estudo do Tratamento da Lepra segundo os resultados obtidos em 10 anos de Terapêutica Antileprótica na Leprosaria Central de Gôa.** [The Treatment of Leprosy and its Results at the Central Leprosarium at Gôa.] *Supplement No. 2 to An. Inst. Med. Trop.* Lisbon. 1945, Nov., 147 pp., 1 fig. [246 refs.]

The author of this record has tried to convey so much information in a small space that the whole is condensed to such a degree as to be almost a catalogue. His original proposition was to write three separate works :—(1) Preparatory treatment of lepers. (2) Treatment of leprosy itself. (3) Treatment of the complications of leprosy. In the present publication the two first are dealt with ; presumably the third will come later. All his statements are amply documented by references to the work and reports of others. A list of 246

references to writers of all nationalities is given and more than half (129) are to abstracts which have appeared in the *Tropical Diseases Bulletin*, indicating how useful foreign writers find this publication.

In the first part, which occupies one-third of the thesis, the preparatory treatment is considered and discussed, attention being drawn to obtaining the hearty co-operation of the patient, seeing to his food and nutrition, to his physical exercise, his mental occupation and distractions, and the treatment of concomitant or intercurrent disease, such as malaria, scabies, influenza, etc.

The Central Leprosarium of Gôa (India) was opened in May 1932, in a fairly isolated rural spot, Macasana, in the Salcete Municipality, and it is divided into two parts, one occupied by the lepers, the other by the staff, their families and dependants. At present there are 100 resident patients. In 1935 there was an outbreak of malaria and 34 of the lepers were attacked. The malaria did not seem to affect the leprotic infection in any way, nor *vice versa*. Twenty-four received vaccination against smallpox and in 15 of them the small operation was followed by a leprotic reaction—aggravation of lesions, especially those of the nerves, and the nodules and glands swelled—which led to much debility and prolonged time of convalescence ; in half the patients the vaccinia pustule became an ulcer which, in some cases, took several weeks to heal ; this was specially noted in those who showed a marked leprous reaction.

In the second part the author considers the many forms of treatment tried in leprosy He deals in turn with chaulmoogra, the oil and its derivatives ; its administration *per os*, *per cutem*, intramuscularly and by the blood-stream, the use of the whole oil and of its ethyl esters, and of the combination of chaulmoogra with cholesterin. Next, with serum therapy, Reenstierna's serum and antitetanus serum, with vaccine therapy, vitamins, sulphonamides, venoms, dyes and chemotherapy. Abundant quotations from the literature are given on each of these, and then remarks on the cases in which the author has himself tried the method. The numbers are, as a rule, too small to be of any statistical value in gauging results, but when added to those of others they may be of some value and anyway are an expression of the opinion of the author.

For oral administration refined chaulmoogra oil is given in gelatin capsules, containing 30 minims each. For the first week in each month one capsule daily is prescribed, for the second and third weeks two capsules daily, for the fourth week none. The cutaneous route is objectionable because of the odour imparted to the body and clothes. Intramuscular injection is the favourite mode of administration and three cases are quoted : one received 33 injections in seven months, when death took place, by which time " the leprosy had slightly improved." A second had only two injections when the onset of cardiac disturbances necessitated a stop ; the third had 25 injections and was slightly improved. For ethyl ester injections the author used E.C.C.O.—ethyl esters of the oil of *H. wightiana* 1 cc., camphor 1 gm., doubly distilled creosote 1 cc. and olive oil 2·5 cc. This is the method chiefly used in the Gôa leprosarium. Three cases are quoted : one man received 377 injections and then died. The drug had no effect on his disease. A second received 25 injections in 4½ months, together with Moogrol and was " clinically cured," but was continuing treatment ; a third was treated similarly and had improved. Sixty-two patients were treated with intravenous injections (up to 70 injections) of Alepol ; 11 of them improved, 5 became worse and 46 remained in their original state.

Ten lepers were given the Reenstierna serum in three or four series of 2–3 intramuscular injections with 5–10-week intervals between the series. The injections were followed by considerable physical depression in all ; three improved, one was worse and six remained unaffected.

One case is recorded, of a patient who developed symptoms of tetanus, trismus, convulsions, opisthotonus, etc., and was given antitetanus serum. To the author's surprise the leprosy nodules shrank, the infiltrations and anaesthetic patches diminished and ulcers cicatrized. [It is a pity that this serum was not tried in other cases to confirm or refute, whether this was purely incidental.]

Eleven were given Vaudremer's vaccine subcutaneously in increasing doses, and good effects were observed in those with oedematous infiltration of hands and feet, with elevation of temperature and general weakness ; for those with eye lesions special caution is to be exercised in its use. Betaxan was found to benefit those with polyneuritis and joint pains in eight patients. Sulphonamide drugs were tried in a few cases, but did not seem to bring about any amelioration. For animal venom the toad (*Bufo bufo*) was tried on some cases of nodular leprosy ; no benefit resulted. The dyes used for treatment were methylene blue (1 per cent. in distilled water, starting with 5 cc. and gradually increasing till 35 cc. might be given at one time) ; brilliant green, crystal violet, trypan blue, fluorescein, eosin, resorcin, gentian violet, erythrosin, fuchsin, acridin, methyl green among others ; the numbers of cases so treated are not stated, but the statement is made that amelioration followed in several.

The author sums up his opinion in the following paragraphs : Chaulmoogra gives the most certain results ; it is best administered in the form of the pure oil neutralized ; good results were also obtained with Leprosan, a product of Taraktogenol A. Alepol was generally disappointing, but seemed to do most good in those of mixed type with skin lesions prominent ; a mixture of chaulmoogra and cholesterin, injected intravenously, is well tolerated, but the practical result is doubtful ; Reenstierna serum proved best in rhinitis cases and those with anaesthetic and infiltrated areas ; Vaudremer's vaccine is specially indicated for those with oedematous infiltrations of the extremities ; toad venom was good in leprous adenitis and neuralgias, in which benefit was often prompt ; sulphonamide drugs find no place in the treatment of leprosy. Vitamin B_1 benefits those with neuralgias and joint pains ; methylene blue caused disappearance of large dyschromic blotches, but had no effect on a nodular case ; mercurochrome intravenously was of benefit in lepromatous ulcers. *H. Harold Scott.*

Mooser, Hermann. [Professor an der Universität Zurich.] **Die Beziehungen des murinen Fleckfiebers zum klassischen Fleckfieber.** [The Relationship of the Murine Typhus Fevers to Classical Typhus.] *Acta Tropica.* Basel. 1945. Suppl. 4. 87 pp., 1 pl. & 1 chart. [171 refs.]

In this volume of 87 pages, including a bibliography of 171 references, the author recapitulates his reasons for holding the following views :—(1) Contrary to the opinion of Nicolle there is only one murine typhus. (2) The differences between *Rickettsia prowazeki* and *R. mooseri* are quantitative and not qualitative. (3) These differences, however, are regularly observed and must be regarded as specific.

The quantitative differences are regarded as being : heterologous protection with vaccines, scrotal phenomenon in the guineapig, pathogenicity for white mice, and serial transfer in mice and rats. In these respects there is merely a disproportion between the pathogenicity and serological activity of the two strains. Some strains of classic typhus cause scrotal lesions in guineapigs, and some can be transferred in series through white mice when large doses of infecting material are used.

Contrary to the claims of Nicolle and Giroud, *R. mooseri* develops in lice exactly as does *R. prowazeki*, and there is no difference between the two with respect to their multiplication in fleas.

The assumption that classical typhus has originated from murine typhus remains an unproved hypothesis, and those who refuse to accept this hypothesis can choose between ZINSSER's view that infection is carried over in inter-epidemic periods by late relapses, and the assumption of Polish workers that the carry-over is by dried faeces of infected lice. Nicolle's hypothesis of a carry-over by inapparent infection is regarded as having been disproved by the author's work in Mexico.

The author again suggests that fleas may play a part in maintaining *R. prowazeki* outside the human body and so in maintaining infection during inter-epidemic periods. In support of this view are the facts that the organism multiplies just as readily in fleas as does *R. mooseri*, and that the life span of the fleas is not shortened by the infection.

Great stress is laid on the importance of the work done by the author and his colleagues in Mexico in throwing light on the significance of the " rickettsia bodies " which are stated to have been of a doubtful nature till 1931. [It seems surprising that serious doubts could have been entertained on this subject after the appearance of the classical work of WOLBACH and his colleagues (see this *Bulletin*, 1922, v. 19, 448) in and before 1922.]

The author claims that much of the recent work on the rickettsiae is merely a rediscovery of the findings made earlier in Mexico and the U.S.A.

The general tone of the book is sharply critical, especially of Nicolle and Zinsser, who, unhappily, are dead. But although this unfortunate circumstance puts the author in an invidious position, he cannot be blamed for speaking plainly in the interests of what he regards as scientific truth. A disturbing impression conveyed by the book is that some widely accepted generalizations connected with epidemic and murine typhus are shown to have been based on inadequate and slender evidence.

No reference is made to the important recent work on the complement-fixation and rickettsia-agglutination reactions in epidemic and murine typhus, but this could hardly be expected in a book which consists largely of a vindication of the author's work, about whose importance there can be no dispute.

John W. D. Megaw.

WAR DEPARTMENT: WASHINGTON. **Insect and Rodent Control. Repairs and Utilities.** *War Dept. Technical Manual TM 5-632.* Wash. 1945 Oct., pp. iii+135, 106 figs. [Numerous refs.]

This publication of the United States War Department is of quarto size, printed in large type on good paper and is profusely illustrated with photographs and diagrams. Short descriptions of the chief insect and rodent pests and of the various methods of controlling them are given. The insect pests include mosquitoes, house flies, bed-bugs, lice, fleas, ticks, " chiggers " (mites), termites (white ants), cockroaches, beetles and ants; the rodents are rats, mice, ground squirrels and pocket gophers; moles, coyotes and foxes are also mentioned.

The methods of control described and illustrated are the recognized major and minor sanitary measures—drainage, screening, spraying and oiling, trapping, poisoning, fumigation, and the protection of buildings against rodents and termites.

Emphasis is laid on the importance of co-operation of Army Departments—Medical, the Corps of Engineers and the Quartermaster Corps with each other and with the specialists of the Public Health Services, the Navy Department, the Department of Agriculture and the Department of the Interior.

The book will be interesting and valuable to all who come into contact with these pests as well as those whose duty it is to deal with them.

J. F. Corson.

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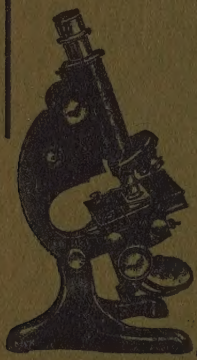

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